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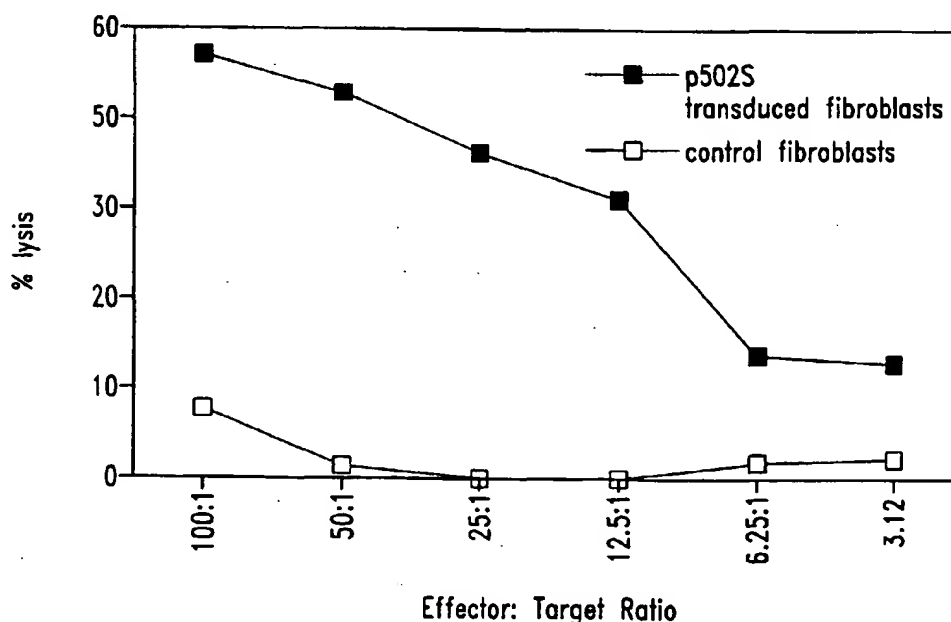
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[Continued on next page]

(54) Title: COMPOSITIONS AND METHODS FOR THE THERAPY AND DIAGNOSIS OF PROSTATE CANCER



(57) Abstract: Compositions and methods for the therapy and diagnosis of cancer, particularly prostate cancer, are disclosed. Illustrative compositions comprise one or more prostate-specific polypeptides, immunogenic portions thereof, polynucleotides that encode such polypeptides, antigen presenting cell that expresses such polypeptides, and T cells that are specific for cells expressing such polypeptides. The disclosed compositions are useful, for example, in the diagnosis, prevention and/or treatment of diseases, particularly prostate cancer.

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## COMPOSITIONS AND METHODS FOR THE THERAPY AND DIAGNOSIS OF PROSTATE CANCER

### TECHNICAL FIELD OF THE INVENTION

The present invention relates generally to therapy and diagnosis of  
5 cancer, such as prostate cancer. The invention is more specifically related to  
polypeptides, comprising at least a portion of a prostate-specific protein, and to  
polynucleotides encoding such polypeptides. Such polypeptides and polynucleotides  
are useful in pharmaceutical compositions, *e.g.*, vaccines, and other compositions for  
the diagnosis and treatment of prostate cancer.

### 10 BACKGROUND OF THE INVENTION

Cancer is a significant health problem throughout the world. Although  
Cancer is a significant health problem throughout the world. Although advances have  
been made in detection and therapy of cancer, no vaccine or other universally successful  
method for prevention or treatment is currently available. Current therapies, which are  
15 generally based on a combination of chemotherapy or surgery and radiation, continue to  
prove inadequate in many patients.

Prostate cancer is the most common form of cancer among males, with  
an estimated incidence of 30% in men over the age of 50. Overwhelming clinical  
evidence shows that human prostate cancer has the propensity to metastasize to bone,  
20 and the disease appears to progress inevitably from androgen dependent to androgen  
refractory status, leading to increased patient mortality. This prevalent disease is  
currently the second leading cause of cancer death among men in the U.S.

In spite of considerable research into therapies for the disease, prostate  
cancer remains difficult to treat. Commonly, treatment is based on surgery and/or  
25 radiation therapy, but these methods are ineffective in a significant percentage of cases.  
Two previously identified prostate specific proteins - prostate specific antigen (PSA)  
and prostatic acid phosphatase (PAP) - have limited therapeutic and diagnostic  
potential. For example, PSA levels do not always correlate well with the presence of

prostate cancer, being positive in a percentage of non-prostate cancer cases, including benign prostatic hyperplasia (BPH). Furthermore, PSA measurements correlate with prostate volume, and do not indicate the level of metastasis.

In spite of considerable research into therapies for these and other  
5 cancers, prostate cancer remains difficult to diagnose and treat effectively. Accordingly, there is a need in the art for improved methods for detecting and treating such cancers. The present invention fulfills these needs and further provides other related advantages.

#### SUMMARY OF THE INVENTION

In one aspect, the present invention provides polynucleotide  
10 compositions comprising a sequence selected from the group consisting of:

(a) sequences provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and  
15 942;

(b) complements of the sequences provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-  
20 931, 938, 939 and 942;

(c) sequences consisting of at least 20 contiguous residues of a sequence provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942;  
25

(d) sequences that hybridize to a sequence provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-

606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942, under moderately stringent conditions;

(e) sequences having at least 75% identity to a sequence of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942;

(f) sequences having at least 90% identity to a sequence of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942; and

(g) degenerate variants of a sequence provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942.

In one preferred embodiment, the polynucleotide compositions of the invention are expressed in at least about 20%, more preferably in at least about 30%, and most preferably in at least about 50% of prostate tissue samples tested, at a level that is at least about 2-fold, preferably at least about 5-fold, and most preferably at least about 10-fold higher than that for other normal tissues.

The present invention, in another aspect, provides polypeptide compositions comprising an amino acid sequence that is encoded by a polynucleotide sequence described above.

The present invention further provides polypeptide compositions comprising an amino acid sequence selected from the group consisting of sequences recited in SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586, 588-590, 592, 706-708, 775, 776, 778, 780, 781, 811, 814, 818, 826, 827, 853, 855,

858, 860-862, 866-877, 879, 883-893, 895, 897, 898, 909-915, 920-928, 932-934, 940, 941 and 943.

In certain preferred embodiments, the polypeptides and/or polynucleotides of the present invention are immunogenic, *i.e.*, they are capable of eliciting an immune response, particularly a humoral and/or cellular immune response, as further described herein.

The present invention further provides fragments, variants and/or derivatives of the disclosed polypeptide and/or polynucleotide sequences, wherein the fragments, variants and/or derivatives preferably have a level of immunogenic activity of at least about 50%, preferably at least about 70% and more preferably at least about 90% of the level of immunogenic activity of a polypeptide sequence set forth in SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586, 588-590, 592, 706-708, 775, 776, 778, 780, 781, 811, 814, 818, 826, 827, 853, 855, 858 or 860-862, or a polypeptide sequence encoded by a polynucleotide sequence set forth in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942.

The present invention further provides polynucleotides that encode a polypeptide described above, expression vectors comprising such polynucleotides and host cells transformed or transfected with such expression vectors.

Within other aspects, the present invention provides pharmaceutical compositions comprising a polypeptide or polynucleotide as described above and a physiologically acceptable carrier.

Within a related aspect of the present invention, pharmaceutical compositions, *e.g.*, vaccine compositions, are provided for prophylactic or therapeutic applications. Such compositions generally comprise an immunogenic polypeptide or polynucleotide of the invention and an immunostimulant, such as an adjuvant, together with a physiologically acceptable carrier.

The present invention further provides pharmaceutical compositions that comprise: (a) an antibody or antigen-binding fragment thereof that specifically binds to a polypeptide of the present invention, or a fragment thereof; and (b) a physiologically acceptable carrier.

5           Within further aspects, the present invention provides pharmaceutical compositions comprising: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) a pharmaceutically acceptable carrier or excipient. Illustrative antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B cells.

10           Within related aspects, pharmaceutical compositions are provided that comprise: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) an immunostimulant.

          The present invention further provides, in other aspects, fusion proteins that comprise at least one polypeptide as described above, as well as polynucleotides  
15   encoding such fusion proteins, typically in the form of pharmaceutical compositions, *e.g.*, vaccine compositions, comprising a physiologically acceptable carrier and/or an immunostimulant. The fusions proteins may comprise multiple immunogenic polypeptides or portions/variants thereof, as described herein, and may further comprise one or more polypeptide segments for facilitating and/or enhancing the expression,  
20   purification and/or immunogenicity of the polypeptide(s).

          Within further aspects, the present invention provides methods for stimulating an immune response in a patient, preferably a T cell response in a human patient, comprising administering a pharmaceutical composition described herein. The patient may be afflicted with prostate cancer, in which case the methods provide  
25   treatment for the disease, or a patient considered to be at risk for such a disease may be treated prophylactically.

          Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient a pharmaceutical composition as recited above. The patient may be afflicted

with prostate cancer, in which case the methods provide treatment for the disease, or a patient considered to be at risk for such a disease may be treated prophylactically.

The present invention further provides, within other aspects, methods for removing tumor cells from a biological sample, comprising contacting a biological  
5 sample with T cells that specifically react with a polypeptide of the present invention, wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the polypeptide from the sample.

Within related aspects, methods are provided for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological  
10 sample treated as described above.

Methods are further provided, within other aspects, for stimulating and/or expanding T cells specific for a polypeptide of the present invention, comprising contacting T cells with one or more of: (i) a polypeptide as described above; (ii) a polynucleotide encoding such a polypeptide; and (iii) an antigen presenting cell that  
15 expresses such a polypeptide; under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells. Isolated T cell populations comprising T cells prepared as described above are also provided.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a  
20 patient an effective amount of a T cell population as described above.

The present invention further provides methods for inhibiting the development of a cancer in a patient, comprising the steps of: (a) incubating CD4<sup>+</sup> and/or CD8<sup>+</sup> T cells isolated from a patient with one or more of: (i) a polypeptide comprising at least an immunogenic portion of polypeptide disclosed herein; (ii) a  
25 polynucleotide encoding such a polypeptide; and (iii) an antigen-presenting cell that expressed such a polypeptide; and (b) administering to the patient an effective amount of the proliferated T cells, thereby inhibiting the development of a cancer in the patient. Proliferated cells may, but need not, be cloned prior to administration to the patient.

Within further aspects, the present invention provides methods for  
30 determining the presence or absence of a cancer, preferably a prostate cancer, in a

patient comprising: (a) contacting a biological sample obtained from a patient with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and (c) comparing the amount of polypeptide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within preferred embodiments, the binding agent is an antibody, more preferably a monoclonal antibody.

The present invention also provides, within other aspects, methods for monitoring the progression of a cancer in a patient. Such methods comprise the steps of: (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polypeptide detected in step (c) with the amount detected in step (b), and therefrom monitoring the progression of the cancer in the patient.

The present invention further provides, within other aspects, methods for determining the presence or absence of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide of the present invention; (b) detecting in the sample a level of a polynucleotide, preferably mRNA, that hybridizes to the oligonucleotide; and (c) comparing the level of polynucleotide that hybridizes to the oligonucleotide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within certain embodiments, the amount of mRNA is detected via polymerase chain reaction using, for example, at least one oligonucleotide primer that hybridizes to a polynucleotide of the present invention, or a complement of such a polynucleotide. Within other embodiments, the amount of mRNA is detected using a hybridization technique, employing an oligonucleotide probe that hybridizes to an inventive polynucleotide, or a complement of such a polynucleotide.

In related aspects, methods are provided for monitoring the progression of a cancer in a patient, comprising the steps of: (a) contacting a biological sample

obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide of the present invention; (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the  
5 amount of polynucleotide detected in step (c) with the amount detected in step (b), and therefrom monitoring the progression of the cancer in the patient.

Within further aspects, the present invention provides antibodies, such as monoclonal antibodies, that bind to a polypeptide as described above, as well as diagnostic kits comprising such antibodies. Diagnostic kits comprising one or more  
10 oligonucleotide probes or primers as described above are also provided.

These and other aspects of the present invention will become apparent upon reference to the following detailed description and attached drawings. All references disclosed herein are hereby incorporated by reference in their entirety as if each was incorporated individually.

## 15 BRIEF DESCRIPTION OF THE DRAWINGS AND SEQUENCE IDENTIFIERS

Figure 1 illustrates the ability of T cells to kill fibroblasts expressing the representative prostate-specific polypeptide P502S, as compared to control fibroblasts. The percentage lysis is shown as a series of effector:target ratios, as indicated.

Figures 2A and 2B illustrate the ability of T cells to recognize cells  
20 expressing the representative prostate-specific polypeptide P502S. In each case, the number of  $\gamma$ -interferon spots is shown for different numbers of responders. In Figure 2A, data is presented for fibroblasts pulsed with the P2S-12 peptide, as compared to fibroblasts pulsed with a control E75 peptide. In Figure 2B, data is presented for fibroblasts expressing P502S, as compared to fibroblasts expressing HER-2/*neu*.

25 Figure 3 represents a peptide competition binding assay showing that the P1S#10 peptide, derived from P501S, binds HLA-A2. Peptide P1S#10 inhibits HLA-A2 restricted presentation of fluM58 peptide to CTL clone D150M58 in TNF release bioassay. D150M58 CTL is specific for the HLA-A2 binding influenza matrix peptide fluM58.



Figure 4 illustrates the ability of T cell lines generated from P1S#10 immunized mice to specifically lyse P1S#10-pulsed Jurkat A2Kb targets and P501S-transduced Jurkat A2Kb targets, as compared to EGFP-transduced Jurkat A2Kb. The percent lysis is shown as a series of effector to target ratios, as indicated.

5                Figure 5 illustrates the ability of a T cell clone to recognize and specifically lyse Jurkat A2Kb cells expressing the representative prostate-specific polypeptide P501S, thereby demonstrating that the P1S#10 peptide may be a naturally processed epitope of the P501S polypeptide.

10              Figures 6A and 6B are graphs illustrating the specificity of a CD8<sup>+</sup> cell line (3A-1) for a representative prostate-specific antigen (P501S). Figure 6A shows the results of a <sup>51</sup>Cr release assay. The percent specific lysis is shown as a series of effector:target ratios, as indicated. Figure 6B shows the production of interferon-gamma by 3A-1 cells stimulated with autologous B-LCL transduced with P501S, at varying effector:target ratios as indicated.

15              Figure 7 is a Western blot showing the expression of P501S in baculovirus.

Figure 8 illustrates the results of epitope mapping studies on P501S.

20              Figure 9 is a schematic representation of the P501S protein showing the location of transmembrane domains and predicted intracellular and extracellular domains.

Figure 10 is a genomic map showing the location of the prostate genes P775P, P704P, B305D, P712P and P774P within the Cat Eye Syndrome region of chromosome 22q11.2

25              Figure 11 shows the results of an ELISA assay to determine the specificity of rabbit polyclonal antisera raised against P501S.

Figures 12A(1), 12A(2), 12A(3), and B are the full-length cDNA (SEQ ID NO:777) and predicted amino acid (SEQ ID NO:778) sequences, respectively, for the clone P788P.

SEQ ID NO: 1 is the determined cDNA sequence for F1-13

30              SEQ ID NO: 2 is the determined 3' cDNA sequence for F1-12

SEQ ID NO: 3 is the determined 5' cDNA sequence for F1-12  
SEQ ID NO: 4 is the determined 3' cDNA sequence for F1-16  
SEQ ID NO: 5 is the determined 3' cDNA sequence for H1-1  
SEQ ID NO: 6 is the determined 3' cDNA sequence for H1-9  
5 SEQ ID NO: 7 is the determined 3' cDNA sequence for H1-4  
SEQ ID NO: 8 is the determined 3' cDNA sequence for J1-17  
SEQ ID NO: 9 is the determined 5' cDNA sequence for J1-17  
SEQ ID NO: 10 is the determined 3' cDNA sequence for L1-12  
SEQ ID NO: 11 is the determined 5' cDNA sequence for L1-12  
10 SEQ ID NO: 12 is the determined 3' cDNA sequence for N1-1862  
SEQ ID NO: 13 is the determined 5' cDNA sequence for N1-1862  
SEQ ID NO: 14 is the determined 3' cDNA sequence for J1-13  
SEQ ID NO: 15 is the determined 5' cDNA sequence for J1-13  
SEQ ID NO: 16 is the determined 3' cDNA sequence for J1-19  
15 SEQ ID NO: 17 is the determined 5' cDNA sequence for J1-19  
SEQ ID NO: 18 is the determined 3' cDNA sequence for J1-25  
SEQ ID NO: 19 is the determined 5' cDNA sequence for J1-25  
SEQ ID NO: 20 is the determined 5' cDNA sequence for J1-24  
SEQ ID NO: 21 is the determined 3' cDNA sequence for J1-24  
20 SEQ ID NO: 22 is the determined 5' cDNA sequence for K1-58  
SEQ ID NO: 23 is the determined 3' cDNA sequence for K1-58  
SEQ ID NO: 24 is the determined 5' cDNA sequence for K1-63  
SEQ ID NO: 25 is the determined 3' cDNA sequence for K1-63  
SEQ ID NO: 26 is the determined 5' cDNA sequence for L1-4  
25 SEQ ID NO: 27 is the determined 3' cDNA sequence for L1-4  
SEQ ID NO: 28 is the determined 5' cDNA sequence for L1-14  
SEQ ID NO: 29 is the determined 3' cDNA sequence for L1-14  
SEQ ID NO: 30 is the determined 3' cDNA sequence for J1-12  
SEQ ID NO: 31 is the determined 3' cDNA sequence for J1-16  
30 SEQ ID NO: 32 is the determined 3' cDNA sequence for J1-21

SEQ ID NO: 33 is the determined 3' cDNA sequence for K1-48  
SEQ ID NO: 34 is the determined 3' cDNA sequence for K1-55  
SEQ ID NO: 35 is the determined 3' cDNA sequence for L1-2  
SEQ ID NO: 36 is the determined 3' cDNA sequence for L1-6  
5 SEQ ID NO: 37 is the determined 3' cDNA sequence for N1-1858  
SEQ ID NO: 38 is the determined 3' cDNA sequence for N1-1860  
SEQ ID NO: 39 is the determined 3' cDNA sequence for N1-1861  
SEQ ID NO: 40 is the determined 3' cDNA sequence for N1-1864  
SEQ ID NO: 41 is the determined cDNA sequence for P5  
10 SEQ ID NO: 42 is the determined cDNA sequence for P8  
SEQ ID NO: 43 is the determined cDNA sequence for P9  
SEQ ID NO: 44 is the determined cDNA sequence for P18  
SEQ ID NO: 45 is the determined cDNA sequence for P20  
SEQ ID NO: 46 is the determined cDNA sequence for P29  
15 SEQ ID NO: 47 is the determined cDNA sequence for P30  
SEQ ID NO: 48 is the determined cDNA sequence for P34  
SEQ ID NO: 49 is the determined cDNA sequence for P36  
SEQ ID NO: 50 is the determined cDNA sequence for P38  
SEQ ID NO: 51 is the determined cDNA sequence for P39  
20 SEQ ID NO: 52 is the determined cDNA sequence for P42  
SEQ ID NO: 53 is the determined cDNA sequence for P47  
SEQ ID NO: 54 is the determined cDNA sequence for P49  
SEQ ID NO: 55 is the determined cDNA sequence for P50  
SEQ ID NO: 56 is the determined cDNA sequence for P53  
25 SEQ ID NO: 57 is the determined cDNA sequence for P55  
SEQ ID NO: 58 is the determined cDNA sequence for P60  
SEQ ID NO: 59 is the determined cDNA sequence for P64  
SEQ ID NO: 60 is the determined cDNA sequence for P65  
SEQ ID NO: 61 is the determined cDNA sequence for P73  
30 SEQ ID NO: 62 is the determined cDNA sequence for P75

SEQ ID NO: 63 is the determined cDNA sequence for P76

SEQ ID NO: 64 is the determined cDNA sequence for P79

SEQ ID NO: 65 is the determined cDNA sequence for P84

SEQ ID NO: 66 is the determined cDNA sequence for P68

5       SEQ ID NO: 67 is the determined cDNA sequence for P80 (also referred  
to as P704P)

SEQ ID NO: 68 is the determined cDNA sequence for P82

SEQ ID NO: 69 is the determined cDNA sequence for U1-3064

SEQ ID NO: 70 is the determined cDNA sequence for U1-3065

10       SEQ ID NO: 71 is the determined cDNA sequence for V1-3692

SEQ ID NO: 72 is the determined cDNA sequence for 1A-3905

SEQ ID NO: 73 is the determined cDNA sequence for V1-3686

SEQ ID NO: 74 is the determined cDNA sequence for R1-2330

SEQ ID NO: 75 is the determined cDNA sequence for 1B-3976

15       SEQ ID NO: 76 is the determined cDNA sequence for V1-3679

SEQ ID NO: 77 is the determined cDNA sequence for 1G-4736

SEQ ID NO: 78 is the determined cDNA sequence for 1G-4738

SEQ ID NO: 79 is the determined cDNA sequence for 1G-4741

SEQ ID NO: 80 is the determined cDNA sequence for 1G-4744

20       SEQ ID NO: 81 is the determined cDNA sequence for 1G-4734

SEQ ID NO: 82 is the determined cDNA sequence for 1H-4774

SEQ ID NO: 83 is the determined cDNA sequence for 1H-4781

SEQ ID NO: 84 is the determined cDNA sequence for 1H-4785

SEQ ID NO: 85 is the determined cDNA sequence for 1H-4787

25       SEQ ID NO: 86 is the determined cDNA sequence for 1H-4796

SEQ ID NO: 87 is the determined cDNA sequence for 1I-4807

SEQ ID NO: 88 is the determined cDNA sequence for 1I-4810

SEQ ID NO: 89 is the determined cDNA sequence for 1I-4811

SEQ ID NO: 90 is the determined cDNA sequence for 1J-4876

30       SEQ ID NO: 91 is the determined cDNA sequence for 1K-4884

- SEQ ID NO: 92 is the determined cDNA sequence for 1K-4896
- SEQ ID NO: 93 is the determined cDNA sequence for 1G-4761
- SEQ ID NO: 94 is the determined cDNA sequence for 1G-4762
- SEQ ID NO: 95 is the determined cDNA sequence for 1H-4766
- 5 SEQ ID NO: 96 is the determined cDNA sequence for 1H-4770
- SEQ ID NO: 97 is the determined cDNA sequence for 1H-4771
- SEQ ID NO: 98 is the determined cDNA sequence for 1H-4772
- SEQ ID NO: 99 is the determined cDNA sequence for 1D-4297
- SEQ ID NO: 100 is the determined cDNA sequence for 1D-4309
- 10 SEQ ID NO: 101 is the determined cDNA sequence for 1D.1-4278
- SEQ ID NO: 102 is the determined cDNA sequence for 1D-4288
- SEQ ID NO: 103 is the determined cDNA sequence for 1D-4283
- SEQ ID NO: 104 is the determined cDNA sequence for 1D-4304
- SEQ ID NO: 105 is the determined cDNA sequence for 1D-4296
- 15 SEQ ID NO: 106 is the determined cDNA sequence for 1D-4280
- SEQ ID NO: 107 is the determined full length cDNA sequence for F1-12  
(also referred to as P504S)
- SEQ ID NO: 108 is the predicted amino acid sequence for F1-12
- SEQ ID NO: 109 is the determined full length cDNA sequence for J1-17
- 20 SEQ ID NO: 110 is the determined full length cDNA sequence for L1-12  
(also referred to as P501S)
- SEQ ID NO: 111 is the determined full length cDNA sequence for N1-1862 (also referred to as P503S)
- SEQ ID NO: 112 is the predicted amino acid sequence for J1-17
- 25 SEQ ID NO: 113 is the predicted amino acid sequence for L1-12 (also referred to as P501S)
- SEQ ID NO: 114 is the predicted amino acid sequence for N1-1862 (also referred to as P503S)
- SEQ ID NO: 115 is the determined cDNA sequence for P89
- 30 SEQ ID NO: 116 is the determined cDNA sequence for P90

SEQ ID NO: 117 is the determined cDNA sequence for P92  
SEQ ID NO: 118 is the determined cDNA sequence for P95  
SEQ ID NO: 119 is the determined cDNA sequence for P98  
SEQ ID NO: 120 is the determined cDNA sequence for P102  
5 SEQ ID NO: 121 is the determined cDNA sequence for P110  
SEQ ID NO: 122 is the determined cDNA sequence for P111  
SEQ ID NO: 123 is the determined cDNA sequence for P114  
SEQ ID NO: 124 is the determined cDNA sequence for P115  
SEQ ID NO: 125 is the determined cDNA sequence for P116  
10 SEQ ID NO: 126 is the determined cDNA sequence for P124  
SEQ ID NO: 127 is the determined cDNA sequence for P126  
SEQ ID NO: 128 is the determined cDNA sequence for P130  
SEQ ID NO: 129 is the determined cDNA sequence for P133  
SEQ ID NO: 130 is the determined cDNA sequence for P138  
15 SEQ ID NO: 131 is the determined cDNA sequence for P143  
SEQ ID NO: 132 is the determined cDNA sequence for P151  
SEQ ID NO: 133 is the determined cDNA sequence for P156  
SEQ ID NO: 134 is the determined cDNA sequence for P157  
SEQ ID NO: 135 is the determined cDNA sequence for P166  
20 SEQ ID NO: 136 is the determined cDNA sequence for P176  
SEQ ID NO: 137 is the determined cDNA sequence for P178  
SEQ ID NO: 138 is the determined cDNA sequence for P179  
SEQ ID NO: 139 is the determined cDNA sequence for P185  
SEQ ID NO: 140 is the determined cDNA sequence for P192  
25 SEQ ID NO: 141 is the determined cDNA sequence for P201  
SEQ ID NO: 142 is the determined cDNA sequence for P204  
SEQ ID NO: 143 is the determined cDNA sequence for P208  
SEQ ID NO: 144 is the determined cDNA sequence for P211  
SEQ ID NO: 145 is the determined cDNA sequence for P213  
30 SEQ ID NO: 146 is the determined cDNA sequence for P219

SEQ ID NO: 147 is the determined cDNA sequence for P237  
SEQ ID NO: 148 is the determined cDNA sequence for P239  
SEQ ID NO: 149 is the determined cDNA sequence for P248  
SEQ ID NO: 150 is the determined cDNA sequence for P251  
5 SEQ ID NO: 151 is the determined cDNA sequence for P255  
SEQ ID NO: 152 is the determined cDNA sequence for P256  
SEQ ID NO: 153 is the determined cDNA sequence for P259  
SEQ ID NO: 154 is the determined cDNA sequence for P260  
SEQ ID NO: 155 is the determined cDNA sequence for P263  
10 SEQ ID NO: 156 is the determined cDNA sequence for P264  
SEQ ID NO: 157 is the determined cDNA sequence for P266  
SEQ ID NO: 158 is the determined cDNA sequence for P270  
SEQ ID NO: 159 is the determined cDNA sequence for P272  
SEQ ID NO: 160 is the determined cDNA sequence for P278  
15 SEQ ID NO: 161 is the determined cDNA sequence for P105  
SEQ ID NO: 162 is the determined cDNA sequence for P107  
SEQ ID NO: 163 is the determined cDNA sequence for P137  
SEQ ID NO: 164 is the determined cDNA sequence for P194  
SEQ ID NO: 165 is the determined cDNA sequence for P195  
20 SEQ ID NO: 166 is the determined cDNA sequence for P196  
SEQ ID NO: 167 is the determined cDNA sequence for P220  
SEQ ID NO: 168 is the determined cDNA sequence for P234  
SEQ ID NO: 169 is the determined cDNA sequence for P235  
SEQ ID NO: 170 is the determined cDNA sequence for P243  
25 SEQ ID NO: 171 is the determined cDNA sequence for P703P-DE1  
SEQ ID NO: 172 is the predicted amino acid sequence for P703P-DE1  
SEQ ID NO: 173 is the determined cDNA sequence for P703P-DE2  
SEQ ID NO: 174 is the determined cDNA sequence for P703P-DE6  
SEQ ID NO: 175 is the determined cDNA sequence for P703P-DE13  
30 SEQ ID NO: 176 is the predicted amino acid sequence for P703P-DE13

SEQ ID NO: 177 is the determined cDNA sequence for P703P-DE14

SEQ ID NO: 178 is the predicted amino acid sequence for P703P-DE14

SEQ ID NO: 179 is the determined extended cDNA sequence for 1G-

4736

5

SEQ ID NO: 180 is the determined extended cDNA sequence for 1G-

4738

SEQ ID NO: 181 is the determined extended cDNA sequence for 1G-

4741

SEQ ID NO: 182 is the determined extended cDNA sequence for 1G-

10 4744

SEQ ID NO: 183 is the determined extended cDNA sequence for 1H-

4774

SEQ ID NO: 184 is the determined extended cDNA sequence for 1H-

4781

15

SEQ ID NO: 185 is the determined extended cDNA sequence for 1H-

4785

SEQ ID NO: 186 is the determined extended cDNA sequence for 1H-

4787

SEQ ID NO: 187 is the determined extended cDNA sequence for 1H-

20 4796

SEQ ID NO: 188 is the determined extended cDNA sequence for 1I-

4807

SEQ ID NO: 189 is the determined 3' cDNA sequence for 1I-4810

SEQ ID NO: 190 is the determined 3' cDNA sequence for 1I-4811

25

SEQ ID NO: 191 is the determined extended cDNA sequence for 1J-

4876

SEQ ID NO: 192 is the determined extended cDNA sequence for 1K-

4884

SEQ ID NO: 193 is the determined extended cDNA sequence for 1K-

30 4896



SEQ ID NO: 194 is the determined extended cDNA sequence for 1G-  
4761

SEQ ID NO: 195 is the determined extended cDNA sequence for 1G-  
4762

5 SEQ ID NO: 196 is the determined extended cDNA sequence for 1H-  
4766

SEQ ID NO: 197 is the determined 3' cDNA sequence for 1H-4770  
SEQ ID NO: 198 is the determined 3' cDNA sequence for 1H-4771  
SEQ ID NO: 199 is the determined extended cDNA sequence for 1H-  
10 4772

SEQ ID NO: 200 is the determined extended cDNA sequence for 1D-  
4309

SEQ ID NO: 201 is the determined extended cDNA sequence for 1D.1-  
4278

15 SEQ ID NO: 202 is the determined extended cDNA sequence for 1D-  
4288

SEQ ID NO: 203 is the determined extended cDNA sequence for 1D-  
4283

SEQ ID NO: 204 is the determined extended cDNA sequence for 1D-  
20 4304

SEQ ID NO: 205 is the determined extended cDNA sequence for 1D-  
4296

SEQ ID NO: 206 is the determined extended cDNA sequence for 1D-  
4280

25 SEQ ID NO: 207 is the determined cDNA sequence for 10-d8fwd  
SEQ ID NO: 208 is the determined cDNA sequence for 10-H10con  
SEQ ID NO: 209 is the determined cDNA sequence for 11-C8rev  
SEQ ID NO: 210 is the determined cDNA sequence for 7.g6fwd  
SEQ ID NO: 211 is the determined cDNA sequence for 7.g6rev  
30 SEQ ID NO: 212 is the determined cDNA sequence for 8-b5fwd

SEQ ID NO: 213 is the determined cDNA sequence for 8-b5rev  
SEQ ID NO: 214 is the determined cDNA sequence for 8-b6fwd  
SEQ ID NO: 215 is the determined cDNA sequence for 8-b6 rev  
SEQ ID NO: 216 is the determined cDNA sequence for 8-d4fwd  
5 SEQ ID NO: 217 is the determined cDNA sequence for 8-d9rev  
SEQ ID NO: 218 is the determined cDNA sequence for 8-g3fwd  
SEQ ID NO: 219 is the determined cDNA sequence for 8-g3rev  
SEQ ID NO: 220 is the determined cDNA sequence for 8-h11rev  
SEQ ID NO: 221 is the determined cDNA sequence for g-f12fwd  
10 SEQ ID NO: 222 is the determined cDNA sequence for g-f3rev  
SEQ ID NO: 223 is the determined cDNA sequence for P509S  
SEQ ID NO: 224 is the determined cDNA sequence for P510S  
SEQ ID NO: 225 is the determined cDNA sequence for P703DE5  
SEQ ID NO: 226 is the determined cDNA sequence for 9-A11  
15 SEQ ID NO: 227 is the determined cDNA sequence for 8-C6  
SEQ ID NO: 228 is the determined cDNA sequence for 8-H7  
SEQ ID NO: 229 is the determined cDNA sequence for JPTPN13  
SEQ ID NO: 230 is the determined cDNA sequence for JPTPN14  
SEQ ID NO: 231 is the determined cDNA sequence for JPTPN23  
20 SEQ ID NO: 232 is the determined cDNA sequence for JPTPN24  
SEQ ID NO: 233 is the determined cDNA sequence for JPTPN25  
SEQ ID NO: 234 is the determined cDNA sequence for JPTPN30  
SEQ ID NO: 235 is the determined cDNA sequence for JPTPN34  
SEQ ID NO: 236 is the determined cDNA sequence for PTPN35  
25 SEQ ID NO: 237 is the determined cDNA sequence for JPTPN36  
SEQ ID NO: 238 is the determined cDNA sequence for JPTPN38  
SEQ ID NO: 239 is the determined cDNA sequence for JPTPN39  
SEQ ID NO: 240 is the determined cDNA sequence for JPTPN40  
SEQ ID NO: 241 is the determined cDNA sequence for JPTPN41  
30 SEQ ID NO: 242 is the determined cDNA sequence for JPTPN42

SEQ ID NO: 243 is the determined cDNA sequence for JPTPN45  
SEQ ID NO: 244 is the determined cDNA sequence for JPTPN46  
SEQ ID NO: 245 is the determined cDNA sequence for JPTPN51  
SEQ ID NO: 246 is the determined cDNA sequence for JPTPN56  
5 SEQ ID NO: 247 is the determined cDNA sequence for PTPN64  
SEQ ID NO: 248 is the determined cDNA sequence for JPTPN65  
SEQ ID NO: 249 is the determined cDNA sequence for JPTPN67  
SEQ ID NO: 250 is the determined cDNA sequence for JPTPN76  
SEQ ID NO: 251 is the determined cDNA sequence for JPTPN84  
10 SEQ ID NO: 252 is the determined cDNA sequence for JPTPN85  
SEQ ID NO: 253 is the determined cDNA sequence for JPTPN86  
SEQ ID NO: 254 is the determined cDNA sequence for JPTPN87  
SEQ ID NO: 255 is the determined cDNA sequence for JPTPN88  
SEQ ID NO: 256 is the determined cDNA sequence for JP1F1  
15 SEQ ID NO: 257 is the determined cDNA sequence for JP1F2  
SEQ ID NO: 258 is the determined cDNA sequence for JP1C2  
SEQ ID NO: 259 is the determined cDNA sequence for JP1B1  
SEQ ID NO: 260 is the determined cDNA sequence for JP1B2  
SEQ ID NO: 261 is the determined cDNA sequence for JP1D3  
20 SEQ ID NO: 262 is the determined cDNA sequence for JP1A4  
SEQ ID NO: 263 is the determined cDNA sequence for JP1F5  
SEQ ID NO: 264 is the determined cDNA sequence for JP1E6  
SEQ ID NO: 265 is the determined cDNA sequence for JP1D6  
SEQ ID NO: 266 is the determined cDNA sequence for JP1B5  
25 SEQ ID NO: 267 is the determined cDNA sequence for JP1A6  
SEQ ID NO: 268 is the determined cDNA sequence for JP1E8  
SEQ ID NO: 269 is the determined cDNA sequence for JP1D7  
SEQ ID NO: 270 is the determined cDNA sequence for JP1D9  
SEQ ID NO: 271 is the determined cDNA sequence for JP1C10  
30 SEQ ID NO: 272 is the determined cDNA sequence for JP1A9

SEQ ID NO: 273 is the determined cDNA sequence for JP1F12  
SEQ ID NO: 274 is the determined cDNA sequence for JP1E12  
SEQ ID NO: 275 is the determined cDNA sequence for JP1D11  
SEQ ID NO: 276 is the determined cDNA sequence for JP1C11  
5 SEQ ID NO: 277 is the determined cDNA sequence for JP1C12  
SEQ ID NO: 278 is the determined cDNA sequence for JP1B12  
SEQ ID NO: 279 is the determined cDNA sequence for JP1A12  
SEQ ID NO: 280 is the determined cDNA sequence for JP8G2  
SEQ ID NO: 281 is the determined cDNA sequence for JP8H1  
10 SEQ ID NO: 282 is the determined cDNA sequence for JP8H2  
SEQ ID NO: 283 is the determined cDNA sequence for JP8A3  
SEQ ID NO: 284 is the determined cDNA sequence for JP8A4  
SEQ ID NO: 285 is the determined cDNA sequence for JP8C3  
SEQ ID NO: 286 is the determined cDNA sequence for JP8G4  
15 SEQ ID NO: 287 is the determined cDNA sequence for JP8B6  
SEQ ID NO: 288 is the determined cDNA sequence for JP8D6  
SEQ ID NO: 289 is the determined cDNA sequence for JP8F5  
SEQ ID NO: 290 is the determined cDNA sequence for JP8A8  
SEQ ID NO: 291 is the determined cDNA sequence for JP8C7  
20 SEQ ID NO: 292 is the determined cDNA sequence for JP8D7  
SEQ ID NO: 293 is the determined cDNA sequence for P8D8  
SEQ ID NO: 294 is the determined cDNA sequence for JP8E7  
SEQ ID NO: 295 is the determined cDNA sequence for JP8F8  
SEQ ID NO: 296 is the determined cDNA sequence for JP8G8  
25 SEQ ID NO: 297 is the determined cDNA sequence for JP8B10  
SEQ ID NO: 298 is the determined cDNA sequence for JP8C10  
SEQ ID NO: 299 is the determined cDNA sequence for JP8E9  
SEQ ID NO: 300 is the determined cDNA sequence for JP8E10  
SEQ ID NO: 301 is the determined cDNA sequence for JP8F9  
30 SEQ ID NO: 302 is the determined cDNA sequence for JP8H9

- SEQ ID NO: 303 is the determined cDNA sequence for JP8C12  
SEQ ID NO: 304 is the determined cDNA sequence for JP8E11  
SEQ ID NO: 305 is the determined cDNA sequence for JP8E12  
SEQ ID NO: 306 is the amino acid sequence for the peptide PS2#12  
5 SEQ ID NO: 307 is the determined cDNA sequence for P711P  
SEQ ID NO: 308 is the determined cDNA sequence for P712P  
SEQ ID NO: 309 is the determined cDNA sequence for CLONE23  
SEQ ID NO: 310 is the determined cDNA sequence for P774P  
SEQ ID NO: 311 is the determined cDNA sequence for P775P  
10 SEQ ID NO: 312 is the determined cDNA sequence for P715P  
SEQ ID NO: 313 is the determined cDNA sequence for P710P  
SEQ ID NO: 314 is the determined cDNA sequence for P767P  
SEQ ID NO: 315 is the determined cDNA sequence for P768P  
SEQ ID NO: 316-325 are the determined cDNA sequences of previously  
15 isolated genes  
SEQ ID NO: 326 is the determined cDNA sequence for P703PDE5  
SEQ ID NO: 327 is the predicted amino acid sequence for P703PDE5  
SEQ ID NO: 328 is the determined cDNA sequence for P703P6.26  
SEQ ID NO: 329 is the predicted amino acid sequence for P703P6.26  
20 SEQ ID NO: 330 is the determined cDNA sequence for P703PX-23  
SEQ ID NO: 331 is the predicted amino acid sequence for P703PX-23  
SEQ ID NO: 332 is the determined full length cDNA sequence for  
P509S  
SEQ ID NO: 333 is the determined extended cDNA sequence for P707P  
25 (also referred to as 11-C9)  
SEQ ID NO: 334 is the determined cDNA sequence for P714P  
SEQ ID NO: 335 is the determined cDNA sequence for P705P (also  
referred to as 9-F3)  
SEQ ID NO: 336 is the predicted amino acid sequence for P705P  
30 SEQ ID NO: 337 is the amino acid sequence of the peptide P1S#10

- SEQ ID NO: 338 is the amino acid sequence of the peptide p5
- SEQ ID NO: 339 is the predicted amino acid sequence of P509S
- SEQ ID NO: 340 is the determined cDNA sequence for P778P
- SEQ ID NO: 341 is the determined cDNA sequence for P786P
- 5 SEQ ID NO: 342 is the determined cDNA sequence for P789P
- SEQ ID NO: 343 is the determined cDNA sequence for a clone showing  
homology to Homo sapiens MM46 mRNA
- SEQ ID NO: 344 is the determined cDNA sequence for a clone showing  
homology to Homo sapiens TNF-alpha stimulated ABC protein (ABC50) mRNA
- 10 SEQ ID NO: 345 is the determined cDNA sequence for a clone showing  
homology to Homo sapiens mRNA for E-cadherin
- SEQ ID NO: 346 is the determined cDNA sequence for a clone showing  
homology to Human nuclear-encoded mitochondrial serine hydroxymethyltransferase  
(SHMT)
- 15 SEQ ID NO: 347 is the determined cDNA sequence for a clone showing  
homology to Homo sapiens natural resistance-associated macrophage protein2  
(NRAMP2)
- SEQ ID NO: 348 is the determined cDNA sequence for a clone showing  
homology to Homo sapiens phosphoglucomutase-related protein (PGMRP)
- 20 SEQ ID NO: 349 is the determined cDNA sequence for a clone showing  
homology to Human mRNA for proteosome subunit p40
- SEQ ID NO: 350 is the determined cDNA sequence for P777P
- SEQ ID NO: 351 is the determined cDNA sequence for P779P
- SEQ ID NO: 352 is the determined cDNA sequence for P790P
- 25 SEQ ID NO: 353 is the determined cDNA sequence for P784P
- SEQ ID NO: 354 is the determined cDNA sequence for P776P
- SEQ ID NO: 355 is the determined cDNA sequence for P780P
- SEQ ID NO: 356 is the determined cDNA sequence for P544S
- SEQ ID NO: 357 is the determined cDNA sequence for P745S
- 30 SEQ ID NO: 358 is the determined cDNA sequence for P782P

SEQ ID NO: 359 is the determined cDNA sequence for P783P

SEQ ID NO: 360 is the determined cDNA sequence for unknown 17984

SEQ ID NO: 361 is the determined cDNA sequence for P787P

SEQ ID NO: 362 is the determined cDNA sequence for P788P

5 SEQ ID NO: 363 is the determined cDNA sequence for unknown 17994

SEQ ID NO: 364 is the determined cDNA sequence for P781P

SEQ ID NO: 365 is the determined cDNA sequence for P785P

SEQ ID NO: 366-375 are the determined cDNA sequences for splice variants of B305D.

10 SEQ ID NO: 376 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 366.

SEQ ID NO: 377 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 372.

15 SEQ ID NO: 378 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 373.

SEQ ID NO: 379 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 374.

SEQ ID NO: 380 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 375.

20 SEQ ID NO: 381 is the determined cDNA sequence for B716P.

SEQ ID NO: 382 is the determined full-length cDNA sequence for P711P.

SEQ ID NO: 383 is the predicted amino acid sequence for P711P.

SEQ ID NO: 384 is the cDNA sequence for P1000C.

25 SEQ ID NO: 385 is the cDNA sequence for CGI-82.

SEQ ID NO: 386 is the cDNA sequence for 23320.

SEQ ID NO: 387 is the cDNA sequence for CGI-69.

SEQ ID NO: 388 is the cDNA sequence for L-iditol-2-dehydrogenase.

SEQ ID NO: 389 is the cDNA sequence for 23379.

30 SEQ ID NO: 390 is the cDNA sequence for 23381.

SEQ ID NO:391 is the cDNA sequence for KIAA0122.

SEQ ID NO:392 is the cDNA sequence for 23399.

SEQ ID NO:393 is the cDNA sequence for a previously identified gene.

SEQ ID NO:394 is the cDNA sequence for HCLBP.

5 SEQ ID NO:395 is the cDNA sequence for transglutaminase.

SEQ ID NO:396 is the cDNA sequence for a previously identified gene.

SEQ ID NO:397 is the cDNA sequence for PAP.

SEQ ID NO:398 is the cDNA sequence for Ets transcription factor  
PDEF.

10 SEQ ID NO:399 is the cDNA sequence for hTGR.

SEQ ID NO:400 is the cDNA sequence for KIAA0295.

SEQ ID NO:401 is the cDNA sequence for 22545.

SEQ ID NO:402 is the cDNA sequence for 22547.

SEQ ID NO:403 is the cDNA sequence for 22548.

15 SEQ ID NO:404 is the cDNA sequence for 22550.

SEQ ID NO:405 is the cDNA sequence for 22551.

SEQ ID NO:406 is the cDNA sequence for 22552.

SEQ ID NO:407 is the cDNA sequence for 22553 (also known as  
P1020C).

20 SEQ ID NO:408 is the cDNA sequence for 22558.

SEQ ID NO:409 is the cDNA sequence for 22562.

SEQ ID NO:410 is the cDNA sequence for 22565.

SEQ ID NO:411 is the cDNA sequence for 22567.

SEQ ID NO:412 is the cDNA sequence for 22568.

25 SEQ ID NO:413 is the cDNA sequence for 22570.

SEQ ID NO:414 is the cDNA sequence for 22571.

SEQ ID NO:415 is the cDNA sequence for 22572.

SEQ ID NO:416 is the cDNA sequence for 22573.

SEQ ID NO:417 is the cDNA sequence for 22573.

30 SEQ ID NO:418 is the cDNA sequence for 22575.



SEQ ID NO:419 is the cDNA sequence for 22580.  
SEQ ID NO:420 is the cDNA sequence for 22581.  
SEQ ID NO:421 is the cDNA sequence for 22582.  
SEQ ID NO:422 is the cDNA sequence for 22583.  
5 SEQ ID NO:423 is the cDNA sequence for 22584.  
SEQ ID NO:424 is the cDNA sequence for 22585.  
SEQ ID NO:425 is the cDNA sequence for 22586.  
SEQ ID NO:426 is the cDNA sequence for 22587.  
SEQ ID NO:427 is the cDNA sequence for 22588.  
10 SEQ ID NO:428 is the cDNA sequence for 22589.  
SEQ ID NO:429 is the cDNA sequence for 22590.  
SEQ ID NO:430 is the cDNA sequence for 22591.  
SEQ ID NO:431 is the cDNA sequence for 22592.  
SEQ ID NO:432 is the cDNA sequence for 22593.  
15 SEQ ID NO:433 is the cDNA sequence for 22594.  
SEQ ID NO:434 is the cDNA sequence for 22595.  
SEQ ID NO:435 is the cDNA sequence for 22596.  
SEQ ID NO:436 is the cDNA sequence for 22847.  
SEQ ID NO:437 is the cDNA sequence for 22848.  
20 SEQ ID NO:438 is the cDNA sequence for 22849.  
SEQ ID NO:439 is the cDNA sequence for 22851.  
SEQ ID NO:440 is the cDNA sequence for 22852.  
SEQ ID NO:441 is the cDNA sequence for 22853.  
SEQ ID NO:442 is the cDNA sequence for 22854.  
25 SEQ ID NO:443 is the cDNA sequence for 22855.  
SEQ ID NO:444 is the cDNA sequence for 22856.  
SEQ ID NO:445 is the cDNA sequence for 22857.  
SEQ ID NO:446 is the cDNA sequence for 23601.  
SEQ ID NO:447 is the cDNA sequence for 23602.  
30 SEQ ID NO:448 is the cDNA sequence for 23605.

- SEQ ID NO:449 is the cDNA sequence for 23606.
- SEQ ID NO:450 is the cDNA sequence for 23612.
- SEQ ID NO:451 is the cDNA sequence for 23614.
- SEQ ID NO:452 is the cDNA sequence for 23618.
- 5 SEQ ID NO:453 is the cDNA sequence for 23622.
- SEQ ID NO:454 is the cDNA sequence for folate hydrolase.
- SEQ ID NO:455 is the cDNA sequence for LIM protein.
- SEQ ID NO:456 is the cDNA sequence for a known gene.
- SEQ ID NO:457 is the cDNA sequence for a known gene.
- 10 SEQ ID NO:458 is the cDNA sequence for a previously identified gene.
- SEQ ID NO:459 is the cDNA sequence for 23045.
- SEQ ID NO:460 is the cDNA sequence for 23032.
- SEQ ID NO:461 is the cDNA sequence for clone 23054.
- SEQ ID NO:462-467 are cDNA sequences for known genes.
- 15 SEQ ID NO:468-471 are cDNA sequences for P710P.
- SEQ ID NO:472 is a cDNA sequence for P1001C.
- SEQ ID NO: 473 is the determined cDNA sequence for a first splice variant of P775P (referred to as 27505).
- SEQ ID NO: 474 is the determined cDNA sequence for a second splice variant of P775P (referred to as 19947).
- 20 SEQ ID NO: 475 is the determined cDNA sequence for a third splice variant of P775P (referred to as 19941).
- SEQ ID NO: 476 is the determined cDNA sequence for a fourth splice variant of P775P (referred to as 19937).
- 25 SEQ ID NO: 477 is a first predicted amino acid sequence encoded by the sequence of SEQ ID NO: 474.
- SEQ ID NO: 478 is a second predicted amino acid sequence encoded by the sequence of SEQ ID NO: 474.
- SEQ ID NO: 479 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 475.
- 30

SEQ ID NO: 480 is a first predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

SEQ ID NO: 481 is a second predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

5           SEQ ID NO: 482 is a third predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

SEQ ID NO: 483 is a fourth predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

10           SEQ ID NO: 484 is the first 30 amino acids of the *M. tuberculosis* antigen Ra12.

SEQ ID NO: 485 is the PCR primer AW025.

SEQ ID NO: 486 is the PCR primer AW003.

SEQ ID NO: 487 is the PCR primer AW027.

SEQ ID NO: 488 is the PCR primer AW026.

15           SEQ ID NO: 489-501 are peptides employed in epitope mapping studies.

SEQ ID NO: 502 is the determined cDNA sequence of the complementarity determining region for the anti-P503S monoclonal antibody 20D4.

SEQ ID NO: 503 is the determined cDNA sequence of the complementarity determining region for the anti-P503S monoclonal antibody JA1.

20           SEQ ID NO: 504 & 505 are peptides employed in epitope mapping studies.

SEQ ID NO: 506 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 8H2.

25           SEQ ID NO: 507 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 7H8.

SEQ ID NO: 508 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 2D4.

SEQ ID NO: 509-522 are peptides employed in epitope mapping studies.

30           SEQ ID NO: 523 is a mature form of P703P used to raise antibodies against P703P.

SEQ ID NO: 524 is the putative full-length cDNA sequence of P703P.

SEQ ID NO: 525 is the predicted amino acid sequence encoded by SEQ ID NO: 524.

SEQ ID NO: 526 is the full-length cDNA sequence for P790P.

5 SEQ ID NO: 527 is the predicted amino acid sequence for P790P.

SEQ ID NO: 528 & 529 are PCR primers.

SEQ ID NO: 530 is the cDNA sequence of a splice variant of SEQ ID NO: 366.

10 SEQ ID NO: 531 is the cDNA sequence of the open reading frame of SEQ ID NO: 530.

SEQ ID NO: 532 is the predicted amino acid encoded by the sequence of SEQ ID NO: 531.

SEQ ID NO: 533 is the DNA sequence of a putative ORF of P775P.

15 SEQ ID NO: 534 is the predicted amino acid sequence encoded by SEQ ID NO: 533.

SEQ ID NO: 535 is a first full-length cDNA sequence for P510S.

SEQ ID NO: 536 is a second full-length cDNA sequence for P510S.

SEQ ID NO: 537 is the predicted amino acid sequence encoded by SEQ ID NO: 535.

20 SEQ ID NO: 538 is the predicted amino acid sequence encoded by SEQ ID NO: 536.

SEQ ID NO: 539 is the peptide P501S-370.

SEQ ID NO: 540 is the peptide P501S-376.

SEQ ID NO: 541-551 are epitopes of P501S.

25 SEQ ID NO: 552 is an extended cDNA sequence for P712P.

SEQ ID NO: 553-568 are the amino acid sequences encoded by predicted open reading frames within SEQ ID NO: 552.

SEQ ID NO: 569 is an extended cDNA sequence for P776P.

30 SEQ ID NO: 570 is the determined cDNA sequence for a splice variant of P776P referred to as contig 6.

SEQ ID NO: 571 is the determined cDNA sequence for a splice variant of P776P referred to as contig 7.

SEQ ID NO: 572 is the determined cDNA sequence for a splice variant of P776P referred to as contig 14.

5               SEQ ID NO: 573 is the amino acid sequence encoded by a first predicted ORF of SEQ ID NO: 570.

SEQ ID NO: 574 is the amino acid sequence encoded by a second predicted ORF of SEQ ID NO: 570.

10             SEQ ID NO: 575 is the amino acid sequence encoded by a predicted ORF of SEQ ID NO: 571.

SEQ ID NO: 576-586 are amino acid sequences encoded by predicted ORFs of SEQ ID NO: 569.

SEQ ID NO: 587 is a DNA consensus sequence of the sequences of P767P and P777P.

15             SEQ ID NO: 588-590 are amino acid sequences encoded by predicted ORFs of SEQ ID NO: 587.

SEQ ID NO: 591 is an extended cDNA sequence for P1020C.

SEQ ID NO: 592 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: P1020C.

20             SEQ ID NO: 593 is a splice variant of P775P referred to as 50748.

SEQ ID NO: 594 is a splice variant of P775P referred to as 50717. SEQ ID NO: 595 is a splice variant of P775P referred to as 45985.

SEQ ID NO: 596 is a splice variant of P775P referred to as 38769.

SEQ ID NO: 597 is a splice variant of P775P referred to as 37922.

25             SEQ ID NO: 598 is a splice variant of P510S referred to as 49274.

SEQ ID NO: 599 is a splice variant of P510S referred to as 39487.

SEQ ID NO: 600 is a splice variant of P504S referred to as 5167.16.

SEQ ID NO: 601 is a splice variant of P504S referred to as 5167.1.

SEQ ID NO: 602 is a splice variant of P504S referred to as 5163.46.

30             SEQ ID NO: 603 is a splice variant of P504S referred to as 5163.42.

SEQ ID NO: 604 is a splice variant of P504S referred to as 5163.34.

SEQ ID NO: 605 is a splice variant of P504S referred to as 5163.17.

SEQ ID NO: 606 is a splice variant of P501S referred to as 10640.

SEQ ID NO: 607-615 are the sequences of PCR primers.

5        SEQ ID NO: 616 is the determined cDNA sequence of a fusion of P703P  
and PSA.

SEQ ID NO: 617 is the amino acid sequence of the fusion of P703P and  
PSA.

10       SEQ ID NO: 618-689 are determined cDNA sequences of prostate-  
specific clones.

SEQ ID NO: 690 is the cDNA sequence of the gene DD3.

SEQ ID NO: 691-697 are determined cDNA sequences of prostate-  
specific clones.

SEQ ID NO: 698 is an extended cDNA sequence for P714P.

15       SEQ ID NO: 699-701 are the cDNA sequences for splice variants of  
P704P.

SEQ ID NO: 702 is the cDNA sequence of a spliced variant of P553S  
referred to as P553S-14.

20       SEQ ID NO: 703 is the cDNA sequence of a spliced variant of P553S  
referred to as P553S-12.

SEQ ID NO: 704 is the cDNA sequence of a spliced variant of P553S  
referred to as P553S-10.

SEQ ID NO: 705 is the cDNA sequence of a spliced variant of P553S  
referred to as P553S-6.

25       SEQ ID NO: 706 is the amino acid sequence encoded by SEQ ID NO:  
705.

SEQ ID NO: 707 is the amino acid sequence encoded by SEQ ID NO:  
702 SEQ ID NO: 708 is a second amino acid sequence encoded by SEQ ID NO: 702.

30       SEQ ID NO: 709-772 are determined cDNA sequences of prostate-  
specific clones.

SEQ ID NO: 773 is a first full-length cDNA sequence for prostate-specific transglutaminase gene (also referred to herein as P558S).

SEQ ID NO: 774 is a second full-length cDNA sequence for prostate-specific transglutaminase gene.

5                   SEQ ID NO: 775 is the amino acid sequence encoded by the sequence of  
SEQ ID NO: 773.

SEQ ID NO: 776 is the amino acid sequence encoded by the sequence of  
SEQ ID NO: 774.

SEQ ID NO: 777 is the full-length cDNA sequence for P788P.

10                  SEQ ID NO: 778 is the amino acid sequence encoded by SEQ ID NO:  
777.

SEQ ID NO: 779 is the determined cDNA sequence for a polymorphic  
variant of P788P.

15                  SEQ ID NO: 780 is the amino acid sequence encoded by SEQ ID NO:  
779.

SEQ ID NO: 781 is the amino acid sequence of peptide 4 from P703P.

SEQ ID NO: 782 is the cDNA sequence that encodes peptide 4 from  
P703P.

20                  SEQ ID NO: 783-798 are the cDNA sequence encoding epitopes of  
P703P.

SEQ ID NO: 799-814 are the amino acid sequences of epitopes of  
P703P.

SEQ ID NO: 815 and 816 are PCR primers.

25                  SEQ ID NO: 817 is the cDNA sequence encoding an N-terminal portion  
of P788P expressed in *E. coli*.

SEQ ID NO: 818 is the amino acid sequence of the N-terminal portion of  
P788P expressed in *E. coli*.

SEQ ID NO: 819 is the amino acid sequence of the *M. tuberculosis*  
antigen Ra12.

30                  SEQ ID NO: 820 and 821 are PCR primers.

SEQ ID NO: 822 is the cDNA sequence for the Ra12-P510S-C construct.

SEQ ID NO: 823 is the cDNA sequence for the P510S-C construct.

SEQ ID NO: 824 is the cDNA sequence for the P510S-E3 construct.

5 SEQ ID NO: 825 is the amino acid sequence for the Ra12-P510S-C construct.

SEQ ID NO: 826 is the amino acid sequence for the P510S-C construct.

SEQ ID NO: 827 is the amino acid sequence for the P510S-E3 construct.

SEQ ID NO: 828-833 are PCR primers.

10 SEQ ID NO: 834 is the cDNA sequence of the construct Ra12-P775P-ORF3.

SEQ ID NO: 835 is the amino acid sequence of the construct Ra12-P775P-ORF3.

SEQ ID NO: 836 and 837 are PCR primers.

15 SEQ ID NO: 838 is the determined amino acid sequence for a P703P His tag fusion protein.

SEQ ID NO: 839 is the determined cDNA sequence for a P703P His tag fusion protein.

SEQ ID NO: 840 and 841 are PCR primers.

20 SEQ ID NO: 842 is the determined amino acid sequence for a P705P His tag fusion protein.

SEQ ID NO: 843 is the determined cDNA sequence for a P705P His tag fusion protein.

SEQ ID NO: 844 and 845 are PCR primers.

25 SEQ ID NO: 846 is the determined amino acid sequence for a P711P His tag fusion protein.

SEQ ID NO: 847 is the determined cDNA sequence for a P711P His tag fusion protein.

30 SEQ ID NO: 848 is the amino acid sequence of the *M. tuberculosis* antigen Ra12.



SEQ ID NO: 849 and 850 are PCR primers.

SEQ ID NO: 851 is the determined cDNA sequence for the construct Ra12-P501S-E2.

5       SEQ ID NO: 852 is the determined amino acid sequence for the construct Ra12-P501S-E2.

SEQ ID NO: 853 is the amino acid sequence for an epitope of P501S.

SEQ ID NO: 854 is the DNA sequence encoding SEQ ID NO: 853.

SEQ ID NO: 855 is the amino acid sequence for an epitope of P501S.

SEQ ID NO: 856 is the DNA sequence encoding SEQ ID NO: 855.

10       SEQ ID NO: 857 is a peptide employed in epitope mapping studies.

SEQ ID NO: 858 is the amino acid sequence for an epitope of P501S.

SEQ ID NO: 859 is the DNA sequence encoding SEQ ID NO: 858.

SEQ ID NO: 860-862 are the amino acid sequences for CD4 epitopes of P501S.

15       SEQ ID NO: 863-865 are the DNA sequences encoding the sequences of SEQ ID NO: 860-862.

SEQ ID NO: 866-877 are the amino acid sequences for putative CTL epitopes of P703P.

SEQ ID NO: 878 is the full-length cDNA sequence for P789P.

20       SEQ ID NO: 879 is the amino acid sequence encoded by SEQ ID NO: 878.

SEQ ID NO: 880 is the determined full-length cDNA sequence for the splice variant of P776P referred to as contig 6.

25       SEQ ID NO: 881-882 are determined full-length cDNA sequences for the splice variant of P776P referred to as contig 7.

SEQ ID NO: 883-887 are amino acid sequences encoded by SEQ ID NO: 880.

SEQ ID NO: 888-893 are amino acid sequences encoded by the splice variant of P776P referred to as contig 7.

SEQ ID NO: 894 is the full-length cDNA sequence for human transmembrane protease serine 2.

SEQ ID NO: 895 is the amino acid sequence encoded by SEQ ID NO: 894.

5           SEQ ID NO: 896 is the cDNA sequence encoding the first 209 amino acids of human transmembrane protease serine 2.

SEQ ID NO: 897 is the first 209 amino acids of human transmembrane protease serine 2.

10           SEQ ID NO: 898 is the amino acid sequence of peptide 296-322 of P501S.

SEQ ID NO: 899-902 are PCR primers.

SEQ ID NO: 903 is the determined cDNA sequence of the Vb chain of a T cell receptor for the P501S-specific T cell clone 4E5.

15           SEQ ID NO: 904 is the determined cDNA sequence of the Va chain of a T cell receptor for the P501S-specific T cell clone 4E5.

SEQ ID NO: 905 is the amino acid sequence encoded by SEQ ID NO 903.

SEQ ID NO: 906 is the amino acid sequence encoded by SEQ ID NO 904.

20           SEQ ID NO: 907 is the full-length open reading frame for P768P including stop codon.

SEQ ID NO: 908 is the full-length open reading frame for P768P without stop codon.

25           SEQ ID NO: 909 is the amino acid sequence encoded by SEQ ID NO: 908.

SEQ ID NO: 910-915 are the amino acid sequences for predicted domains of P768P.

SEQ ID NO: 916 is the full-length cDNA sequence of P835P.

30           SEQ ID NO: 917 is the cDNA sequence of the previously identified clone FLJ13581.

SEQ ID NO: 918 is the cDNA sequence of the open reading frame for P835P with stop codon.

SEQ ID NO: 919 is the cDNA sequence of the open reading frame for P835P without stop codon.

5           SEQ ID NO: 920 is the full-length amino acid sequence for P835P.

SEQ ID NO: 921-928 are the amino acid sequences of extracellular and intracellular domains of P835P.

SEQ ID NO: 929 is the full-length cDNA sequence for P1000C.

10           SEQ ID NO: 930 is the cDNA sequence of the open reading frame for P1000C, including stop codon.

SEQ ID NO: 931 is the cDNA sequence of the open reading frame for P1000C, without stop codon.

SEQ ID NO: 932 is the full-length amino acid sequence for P1000C.

SEQ ID NO: 933 is amino acids 1-100 of SEQ ID NO: 932.

15           SEQ ID NO: 934 is amino acids 100-492 of SEQ ID NO: 932.

SEQ ID NO: 935-937 are PCR primers.

SEQ ID NO: 938 is the cDNA sequence of the expressed full-length P767P coding region.

20           SEQ ID NO: 939 is the cDNA sequence of an expressed truncated P767P coding region.

SEQ ID NO: 940 is the amino acid sequence encoded by SEQ ID NO: 939.

SEQ ID NO: 941 is the amino acid sequence encoded by SEQ ID NO: 938.

25           SEQ ID NO: 942 is the DNA sequence of a CD4 epitope of P703P.

SEQ ID NO: 943 is the amino acid sequence of a CD4 epitope of P703P.

## DETAILED DESCRIPTION OF THE INVENTION

The present invention is directed generally to compositions and their use in the therapy and diagnosis of cancer, particularly prostate cancer. As described further below, illustrative compositions of the present invention include, but are not restricted to, polypeptides, particularly immunogenic polypeptides, polynucleotides encoding such polypeptides, antibodies and other binding agents, antigen presenting cells (APCs) and immune system cells (*e.g.*, T cells).

The practice of the present invention will employ, unless indicated specifically to the contrary, conventional methods of virology, immunology, microbiology, molecular biology and recombinant DNA techniques within the skill of the art, many of which are described below for the purpose of illustration. Such techniques are explained fully in the literature. See, *e.g.*, Sambrook, et al. *Molecular Cloning: A Laboratory Manual* (2nd Edition, 1989); Maniatis et al. *Molecular Cloning: A Laboratory Manual* (1982); *DNA Cloning: A Practical Approach*, vol. I & II (D. Glover, ed.); *Oligonucleotide Synthesis* (N. Gait, ed., 1984); *Nucleic Acid Hybridization* (B. Hames & S. Higgins, eds., 1985); *Transcription and Translation* (B. Hames & S. Higgins, eds., 1984); *Animal Cell Culture* (R. Freshney, ed., 1986); Perbal, *A Practical Guide to Molecular Cloning* (1984).

All publications, patents and patent applications cited herein, whether *supra* or *infra*, are hereby incorporated by reference in their entirety.

As used in this specification and the appended claims, the singular forms "a," "an" and "the" include plural references unless the content clearly dictates otherwise.

Polypeptide Compositions

As used herein, the term "polypeptide" is used in its conventional meaning, *i.e.*, as a sequence of amino acids. The polypeptides are not limited to a specific length of the product; thus, peptides, oligopeptides, and proteins are included within the definition of polypeptide, and such terms may be used interchangeably herein unless specifically indicated otherwise. This term also does not refer to or exclude post-

expression modifications of the polypeptide, for example, glycosylations, acetylations, phosphorylations and the like, as well as other modifications known in the art, both naturally occurring and non-naturally occurring. A polypeptide may be an entire protein, or a subsequence thereof. Particular polypeptides of interest in the context of this invention are amino acid subsequences comprising epitopes, i.e., antigenic determinants substantially responsible for the immunogenic properties of a polypeptide and being capable of evoking an immune response.

Particularly illustrative polypeptides of the present invention comprise those encoded by a polynucleotide sequence set forth in any one of SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942, or a sequence that hybridizes under moderately stringent conditions, or, alternatively, under highly stringent conditions, to a polynucleotide sequence set forth in any one of SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942. In specific embodiments, the polypeptides of the invention comprise amino acid sequences as set forth in any one of SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586, 588-590, 592, 706-708, 775, 776, 778, 780, 781, 811, 814, 818, 826, 827, 853, 855, 858, 860-862, 866-877, 879, 883-893, 895, 897, 898, 909-915, 920-928, 932-934, 940, 941 and 943.

The polypeptides of the present invention are sometimes herein referred to as prostate-specific proteins or prostate-specific polypeptides, as an indication that their identification has been based at least in part upon their increased levels of expression in prostate tissue samples. Thus, a "prostate-specific polypeptide" or "prostate-specific protein," refers generally to a polypeptide sequence of the present invention, or a polynucleotide sequence encoding such a polypeptide, that is expressed

in a substantial proportion of prostate tissue samples, for example preferably greater than about 20%, more preferably greater than about 30%, and most preferably greater than about 50% or more of prostate tissue samples tested, at a level that is at least two fold, and preferably at least five fold, greater than the level of expression in other normal tissues, as determined using a representative assay provided herein. A prostate-specific polypeptide sequence of the invention, based upon its increased level of expression in tumor cells, has particular utility both as a diagnostic marker as well as a therapeutic target, as further described below.

In certain preferred embodiments, the polypeptides of the invention are immunogenic, *i.e.*, they react detectably within an immunoassay (such as an ELISA or T-cell stimulation assay) with antisera and/or T-cells from a patient with prostate cancer. Screening for immunogenic activity can be performed using techniques well known to the skilled artisan. For example, such screens can be performed using methods such as those described in Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In one illustrative example, a polypeptide may be immobilized on a solid support and contacted with patient sera to allow binding of antibodies within the sera to the immobilized polypeptide. Unbound sera may then be removed and bound antibodies detected using, for example, <sup>125</sup>I-labeled Protein A.

As would be recognized by the skilled artisan, immunogenic portions of the polypeptides disclosed herein are also encompassed by the present invention. An "immunogenic portion," as used herein, is a fragment of an immunogenic polypeptide of the invention that itself is immunologically reactive (*i.e.*, specifically binds) with the B-cells and/or T-cell surface antigen receptors that recognize the polypeptide. Immunogenic portions may generally be identified using well known techniques, such as those summarized in Paul, *Fundamental Immunology*, 3rd ed., 243-247 (Raven Press, 1993) and references cited therein. Such techniques include screening polypeptides for the ability to react with antigen-specific antibodies, antisera and/or T-cell lines or clones. As used herein, antisera and antibodies are "antigen-specific" if they specifically bind to an antigen (*i.e.*, they react with the protein in an ELISA or other

immunoassay, and do not react detectably with unrelated proteins). Such antisera and antibodies may be prepared as described herein, and using well-known techniques.

In one preferred embodiment, an immunogenic portion of a polypeptide of the present invention is a portion that reacts with antisera and/or T-cells at a level that is not substantially less than the reactivity of the full-length polypeptide (*e.g.*, in an ELISA and/or T-cell reactivity assay). Preferably, the level of immunogenic activity of the immunogenic portion is at least about 50%, preferably at least about 70% and most preferably greater than about 90% of the immunogenicity for the full-length polypeptide. In some instances, preferred immunogenic portions will be identified that have a level of immunogenic activity greater than that of the corresponding full-length polypeptide, *e.g.*, having greater than about 100% or 150% or more immunogenic activity.

In certain other embodiments, illustrative immunogenic portions may include peptides in which an N-terminal leader sequence and/or transmembrane domain has been deleted. Other illustrative immunogenic portions will contain a small N- and/or C-terminal deletion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids), relative to the mature protein.

In another embodiment, a polypeptide composition of the invention may also comprise one or more polypeptides that are immunologically reactive with T cells and/or antibodies generated against a polypeptide of the invention, particularly a polypeptide having an amino acid sequence disclosed herein, or to an immunogenic fragment or variant thereof.

In another embodiment of the invention, polypeptides are provided that comprise one or more polypeptides that are capable of eliciting T cells and/or antibodies that are immunologically reactive with one or more polypeptides described herein, or one or more polypeptides encoded by contiguous nucleic acid sequences contained in the polynucleotide sequences disclosed herein, or immunogenic fragments or variants thereof, or to one or more nucleic acid sequences which hybridize to one or more of these sequences under conditions of moderate to high stringency.

The present invention, in another aspect, provides polypeptide fragments comprising at least about 5, 10, 15, 20, 25, 50, or 100 contiguous amino acids, or more, including all intermediate lengths, of a polypeptide composition set forth herein, such as those set forth in SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586, 588-590, 592, 706-708, 775, 776, 778, 780, 781, 811, 814, 818, 826, 827, 853, 855, 858, 860-862, 866-877, 879, 883-893, 895, 897, 898, 909-915, 920-928, 932-934, 940, 941 and 943, or those encoded by a polynucleotide sequence set forth in a sequence of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942.

In another aspect, the present invention provides variants of the polypeptide compositions described herein. Polypeptide variants generally encompassed by the present invention will typically exhibit at least about 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% or more identity (determined as described below), along its length, to a polypeptide sequence set forth herein.

In one preferred embodiment, the polypeptide fragments and variants provided by the present invention are immunologically reactive with an antibody and/or T-cell that reacts with a full-length polypeptide specifically set forth herein.

In another preferred embodiment, the polypeptide fragments and variants provided by the present invention exhibit a level of immunogenic activity of at least about 50%, preferably at least about 70%, and most preferably at least about 90% or more of that exhibited by a full-length polypeptide sequence specifically set forth herein.

A polypeptide "variant," as the term is used herein, is a polypeptide that typically differs from a polypeptide specifically disclosed herein in one or more substitutions, deletions, additions and/or insertions. Such variants may be naturally occurring or may be synthetically generated, for example, by modifying one or more of



the above polypeptide sequences of the invention and evaluating their immunogenic activity as described herein using any of a number of techniques well known in the art.

For example, certain illustrative variants of the polypeptides of the invention include those in which one or more portions, such as an N-terminal leader  
5 sequence or transmembrane domain, have been removed. Other illustrative variants include variants in which a small portion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids) has been removed from the N- and/or C-terminal of the mature protein.

In many instances, a variant will contain conservative substitutions. A "conservative substitution" is one in which an amino acid is substituted for another  
10 amino acid that has similar properties, such that one skilled in the art of peptide chemistry would expect the secondary structure and hydropathic nature of the polypeptide to be substantially unchanged. As described above, modifications may be made in the structure of the polynucleotides and polypeptides of the present invention and still obtain a functional molecule that encodes a variant or derivative polypeptide  
15 with desirable characteristics, *e.g.*, with immunogenic characteristics. When it is desired to alter the amino acid sequence of a polypeptide to create an equivalent, or even an improved, immunogenic variant or portion of a polypeptide of the invention, one skilled in the art will typically change one or more of the codons of the encoding DNA sequence according to Table 1.

20 For example, certain amino acids may be substituted for other amino acids in a protein structure without appreciable loss of interactive binding capacity with structures such as, for example, antigen-binding regions of antibodies or binding sites on substrate molecules. Since it is the interactive capacity and nature of a protein that defines that protein's biological functional activity, certain amino acid sequence  
25 substitutions can be made in a protein sequence, and, of course, its underlying DNA coding sequence, and nevertheless obtain a protein with like properties. It is thus contemplated that various changes may be made in the peptide sequences of the disclosed compositions, or corresponding DNA sequences which encode said peptides without appreciable loss of their biological utility or activity.

TABLE 1

Amino Acids			Codons						
Alanine	Ala	A	GCA	GCC	GCG	GCU			
Cysteine	Cys	C	UGC	UGU					
Aspartic acid	Asp	D	GAC	GAU					
Glutamic acid	Glu	E	GAA	GAG					
Phenylalanine	Phe	F	UUC	UUU					
Glycine	Gly	G	GGA	GGC	GGG	GGU			
Histidine	His	H	CAC	CAU					
Isoleucine	Ile	I	AUA	AUC	AUU				
Lysine	Lys	K	AAA	AAG					
Leucine	Leu	L	UUA	UUG	CUA	CUC	CUG	CUU	
Methionine	Met	M	AUG						
Asparagine	Asn	N	AAC	AAU					
Proline	Pro	P	CCA	CCC	CCG	CCU			
Glutamine	Gln	Q	CAA	CAG					
Arginine	Arg	R	AGA	AGG	CGA	CGC	CGG	CGU	
Serine	Ser	S	AGC	AGU	UCA	UCC	UCG	UCU	
Threonine	Thr	T	ACA	ACC	ACG	ACU			
Valine	Val	V	GUA	GUC	GUG	GUU			
Tryptophan	Trp	W	UGG						
Tyrosine	Tyr	Y	UAC	UAU					

In making such changes, the hydropathic index of amino acids may be considered. The importance of the hydropathic amino acid index in conferring interactive biologic function on a protein is generally understood in the art (Kyte and Doolittle, 1982, incorporated herein by reference). It is accepted that the relative hydropathic character of the amino acid contributes to the secondary structure of the resultant protein, which in turn defines the interaction of the protein with other molecules, for example, enzymes, substrates, receptors, DNA, antibodies, antigens, and the like. Each amino acid has been assigned a hydropathic index on the basis of its

hydrophobicity and charge characteristics (Kyte and Doolittle, 1982). These values are: isoleucine (+4.5); valine (+4.2); leucine (+3.8); phenylalanine (+2.8); cysteine/cystine (+2.5); methionine (+1.9); alanine (+1.8); glycine (−0.4); threonine (−0.7); serine (−0.8); tryptophan (−0.9); tyrosine (−1.3); proline (−1.6); histidine (−3.2); glutamate (−3.5);  
5 glutamine (−3.5); aspartate (−3.5); asparagine (−3.5); lysine (−3.9); and arginine (−4.5).

It is known in the art that certain amino acids may be substituted by other amino acids having a similar hydropathic index or score and still result in a protein with similar biological activity, *i.e.* still obtain a biological functionally equivalent protein. In making such changes, the substitution of amino acids whose hydropathic indices are  
10 within  $\pm 2$  is preferred, those within  $\pm 1$  are particularly preferred, and those within  $\pm 0.5$  are even more particularly preferred. It is also understood in the art that the substitution of like amino acids can be made effectively on the basis of hydrophilicity. U. S. Patent 4,554,101 (specifically incorporated herein by reference in its entirety), states that the greatest local average hydrophilicity of a protein, as governed by the hydrophilicity of  
15 its adjacent amino acids, correlates with a biological property of the protein.

As detailed in U. S. Patent 4,554,101, the following hydrophilicity values have been assigned to amino acid residues: arginine (+3.0); lysine (+3.0); aspartate (+3.0  $\pm$  1); glutamate (+3.0  $\pm$  1); serine (+0.3); asparagine (+0.2); glutamine (+0.2); glycine (0); threonine (−0.4); proline (−0.5  $\pm$  1); alanine (−0.5); histidine (−0.5); cysteine  
20 (−1.0); methionine (−1.3); valine (−1.5); leucine (−1.8); isoleucine (−1.8); tyrosine (−2.3); phenylalanine (−2.5); tryptophan (−3.4). It is understood that an amino acid can be substituted for another having a similar hydrophilicity value and still obtain a biologically equivalent, and in particular, an immunologically equivalent protein. In such changes, the substitution of amino acids whose hydrophilicity values are within  $\pm 2$   
25 is preferred, those within  $\pm 1$  are particularly preferred, and those within  $\pm 0.5$  are even more particularly preferred.

As outlined above, amino acid substitutions are generally therefore based on the relative similarity of the amino acid side-chain substituents, for example, their hydrophobicity, hydrophilicity, charge, size, and the like. Exemplary substitutions that  
30 take various of the foregoing characteristics into consideration are well known to those

of skill in the art and include: arginine and lysine; glutamate and aspartate; serine and threonine; glutamine and asparagine; and valine, leucine and isoleucine.

In addition, any polynucleotide may be further modified to increase stability *in vivo*. Possible modifications include, but are not limited to, the addition of  
5 flanking sequences at the 5' and/or 3' ends; the use of phosphorothioate or 2' O-methyl rather than phosphodiesterase linkages in the backbone; and/or the inclusion of nontraditional bases such as inosine, queosine and wybutosine, as well as acetyl-methyl-, thio- and other modified forms of adenine, cytidine, guanine, thymine and uridine.

10 Amino acid substitutions may further be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity and/or the amphipathic nature of the residues. For example, negatively charged amino acids include aspartic acid and glutamic acid; positively charged amino acids include lysine and arginine; and amino acids with uncharged polar head groups having similar hydrophilicity values  
15 include leucine, isoleucine and valine; glycine and alanine; asparagine and glutamine; and serine, threonine, phenylalanine and tyrosine. Other groups of amino acids that may represent conservative changes include: (1) ala, pro, gly, glu, asp, gln, asn, ser, thr; (2) cys, ser, tyr, thr; (3) val, ile, leu, met, ala, phe; (4) lys, arg, his; and (5) phe, tyr, trp, his. A variant may also, or alternatively, contain nonconservative changes. In a  
20 preferred embodiment, variant polypeptides differ from a native sequence by substitution, deletion or addition of five amino acids or fewer. Variants may also (or alternatively) be modified by, for example, the deletion or addition of amino acids that have minimal influence on the immunogenicity, secondary structure and hydrophobic nature of the polypeptide.

25 As noted above, polypeptides may comprise a signal (or leader) sequence at the N-terminal end of the protein, which co-translationally or post-translationally directs transfer of the protein. The polypeptide may also be conjugated to a linker or other sequence for ease of synthesis, purification or identification of the polypeptide (e.g., poly-His), or to enhance binding of the polypeptide to a solid support. For  
30 example, a polypeptide may be conjugated to an immunoglobulin Fc region.

When comparing polypeptide sequences, two sequences are said to be “identical” if the sequence of amino acids in the two sequences is the same when aligned for maximum correspondence, as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A “comparison window” as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

- Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins – Matrices for detecting distant relationships. In Dayhoff, M.O. (ed.) *Atlas of Protein Sequence and Structure*, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenies pp. 626-645 *Methods in Enzymology* vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) *CABIOS* 5:151-153; Myers, E.W. and Muller W. (1988) *CABIOS* 4:11-17; Robinson, E.D. (1971) *Comb. Theor* 11:105; Santou, N. Nes, M. (1987) *Mol. Biol. Evol.* 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy*, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) *Proc. Natl. Acad. Sci. USA* 80:726-730.

- Alternatively, optimal alignment of sequences for comparison may be conducted by the local identity algorithm of Smith and Waterman (1981) *Add. APL. Math* 2:482, by the identity alignment algorithm of Needleman and Wunsch (1970) *J. Mol. Biol.* 48:443, by the search for similarity methods of Pearson and Lipman (1988) *Proc. Natl. Acad. Sci. USA* 85: 2444, by computerized implementations of these algorithms (GAP, BESTFIT, BLAST, FASTA, and TFASTA in the Wisconsin Genetics

Software Package, Genetics Computer Group (GCG), 575 Science Dr., Madison, WI), or by inspection.

One preferred example of algorithms that are suitable for determining percent sequence identity and sequence similarity are the BLAST and BLAST 2.0 algorithms, which are described in Altschul et al. (1977) *Nucl. Acids Res.* 25:3389-3402 and Altschul et al. (1990) *J. Mol. Biol.* 215:403-410, respectively. BLAST and BLAST 2.0 can be used, for example with the parameters described herein, to determine percent sequence identity for the polynucleotides and polypeptides of the invention. Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information. For amino acid sequences, a scoring matrix can be used to calculate the cumulative score. Extension of the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters W, T and X determine the sensitivity and speed of the alignment.

In one preferred approach, the "percentage of sequence identity" is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polypeptide sequence in the comparison window may comprise additions or deletions (*i.e.*, gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (*i.e.*, the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

Within other illustrative embodiments, a polypeptide may be a fusion polypeptide that comprises multiple polypeptides as described herein, or that comprises at least one polypeptide as described herein and an unrelated sequence, such as a known

tumor protein. A fusion partner may, for example, assist in providing T helper epitopes (an immunological fusion partner), preferably T helper epitopes recognized by humans, or may assist in expressing the protein (an expression enhancer) at higher yields than the native recombinant protein. Certain preferred fusion partners are both immunological and expression enhancing fusion partners. Other fusion partners may be selected so as to increase the solubility of the polypeptide or to enable the polypeptide to be targeted to desired intracellular compartments. Still further fusion partners include affinity tags, which facilitate purification of the polypeptide.

Fusion polypeptides may generally be prepared using standard techniques, including chemical conjugation. Preferably, a fusion polypeptide is expressed as a recombinant polypeptide, allowing the production of increased levels, relative to a non-fused polypeptide, in an expression system. Briefly, DNA sequences encoding the polypeptide components may be assembled separately, and ligated into an appropriate expression vector. The 3' end of the DNA sequence encoding one polypeptide component is ligated, with or without a peptide linker, to the 5' end of a DNA sequence encoding the second polypeptide component so that the reading frames of the sequences are in phase. This permits translation into a single fusion polypeptide that retains the biological activity of both component polypeptides.

A peptide linker sequence may be employed to separate the first and second polypeptide components by a distance sufficient to ensure that each polypeptide folds into its secondary and tertiary structures. Such a peptide linker sequence is incorporated into the fusion polypeptide using standard techniques well known in the art. Suitable peptide linker sequences may be chosen based on the following factors: (1) their ability to adopt a flexible extended conformation; (2) their inability to adopt a secondary structure that could interact with functional epitopes on the first and second polypeptides; and (3) the lack of hydrophobic or charged residues that might react with the polypeptide functional epitopes. Preferred peptide linker sequences contain Gly, Asn and Ser residues. Other near neutral amino acids, such as Thr and Ala may also be used in the linker sequence. Amino acid sequences which may be usefully employed as linkers include those disclosed in Maratea et al., *Gene* 40:39-46, 1985; Murphy et al.,

*Proc. Natl. Acad. Sci. USA* 83:8258-8262, 1986; U.S. Patent No. 4,935,233 and U.S. Patent No. 4,751,180. The linker sequence may generally be from 1 to about 50 amino acids in length. Linker sequences are not required when the first and second polypeptides have non-essential N-terminal amino acid regions that can be used to  
5 separate the functional domains and prevent steric interference.

The ligated DNA sequences are operably linked to suitable transcriptional or translational regulatory elements. The regulatory elements responsible for expression of DNA are located only 5' to the DNA sequence encoding the first polypeptides. Similarly, stop codons required to end translation and  
10 transcription termination signals are only present 3' to the DNA sequence encoding the second polypeptide.

The fusion polypeptide can comprise a polypeptide as described herein together with an unrelated immunogenic protein, such as an immunogenic protein capable of eliciting a recall response. Examples of such proteins include tetanus,  
15 tuberculosis and hepatitis proteins (*see*, for example, Stoute et al. *New Engl. J. Med.*, 336:86-91, 1997).

In one preferred embodiment, the immunological fusion partner is derived from a *Mycobacterium* sp., such as a *Mycobacterium tuberculosis*-derived Ra12 fragment. Ra12 compositions and methods for their use in enhancing the expression  
20 and/or immunogenicity of heterologous polynucleotide/polypeptide sequences is described in U.S. Patent Application 60/158,585, the disclosure of which is incorporated herein by reference in its entirety. Briefly, Ra12 refers to a polynucleotide region that is a subsequence of a *Mycobacterium tuberculosis* MTB32A nucleic acid. MTB32A is a serine protease of 32 KD molecular weight encoded by a gene in virulent  
25 and avirulent strains of *M. tuberculosis*. The nucleotide sequence and amino acid sequence of MTB32A have been described (for example, U.S. Patent Application 60/158,585; *see also*, Skeiky et al., *Infection and Immun.* (1999) 67:3998-4007, incorporated herein by reference). C-terminal fragments of the MTB32A coding sequence express at high levels and remain as a soluble polypeptides throughout the  
30 purification process. Moreover, Ra12 may enhance the immunogenicity of heterologous



immunogenic polypeptides with which it is fused. One preferred Ra12 fusion polypeptide comprises a 14 KD C-terminal fragment corresponding to amino acid residues 192 to 323 of MTB32A. Other preferred Ra12 polynucleotides generally comprise at least about 15 consecutive nucleotides, at least about 30 nucleotides, at least about 60 nucleotides, at least about 100 nucleotides, at least about 200 nucleotides, or at least about 300 nucleotides that encode a portion of a Ra12 polypeptide. Ra12 polynucleotides may comprise a native sequence (*i.e.*, an endogenous sequence that encodes a Ra12 polypeptide or a portion thereof) or may comprise a variant of such a sequence. Ra12 polynucleotide variants may contain one or more substitutions, additions, deletions and/or insertions such that the biological activity of the encoded fusion polypeptide is not substantially diminished, relative to a fusion polypeptide comprising a native Ra12 polypeptide. Variants preferably exhibit at least about 70% identity, more preferably at least about 80% identity and most preferably at least about 90% identity to a polynucleotide sequence that encodes a native Ra12 polypeptide or a portion thereof.

Within other preferred embodiments, an immunological fusion partner is derived from protein D, a surface protein of the gram-negative bacterium *Haemophilus influenza B* (WO 91/18926). Preferably, a protein D derivative comprises approximately the first third of the protein (*e.g.*, the first N-terminal 100-110 amino acids), and a protein D derivative may be lipidated. Within certain preferred embodiments, the first 109 residues of a Lipoprotein D fusion partner is included on the N-terminus to provide the polypeptide with additional exogenous T-cell epitopes and to increase the expression level in *E. coli* (thus functioning as an expression enhancer). The lipid tail ensures optimal presentation of the antigen to antigen presenting cells. Other fusion partners include the non-structural protein from influenzae virus, NS1 (hemagglutinin). Typically, the N-terminal 81 amino acids are used, although different fragments that include T-helper epitopes may be used.

In another embodiment, the immunological fusion partner is the protein known as LYTA, or a portion thereof (preferably a C-terminal portion). LYTA is derived from *Streptococcus pneumoniae*, which synthesizes an N-acetyl-L-alanine

amidase known as amidase LYTA (encoded by the *LytA* gene; *Gene* 43:265-292, 1986). LYTA is an autolysin that specifically degrades certain bonds in the peptidoglycan backbone. The C-terminal domain of the LYTA protein is responsible for the affinity to the choline or to some choline analogues such as DEAE. This property has been  
5 exploited for the development of *E. coli* C-LYTA expressing plasmids useful for expression of fusion proteins. Purification of hybrid proteins containing the C-LYTA fragment at the amino terminus has been described (*see Biotechnology* 10:795-798, 1992). Within a preferred embodiment, a repeat portion of LYTA may be incorporated into a fusion polypeptide. A repeat portion is found in the C-terminal region starting at  
10 residue 178. A particularly preferred repeat portion incorporates residues 188-305.

Yet another illustrative embodiment involves fusion polypeptides, and the polynucleotides encoding them, wherein the fusion partner comprises a targeting signal capable of directing a polypeptide to the endosomal/lysosomal compartment, as described in U.S. Patent No. 5,633,234. An immunogenic polypeptide of the invention,  
15 when fused with this targeting signal, will associate more efficiently with MHC class II molecules and thereby provide enhanced in vivo stimulation of CD4<sup>+</sup> T-cells specific for the polypeptide.

Polypeptides of the invention are prepared using any of a variety of well known synthetic and/or recombinant techniques, the latter of which are further  
20 described below. Polypeptides, portions and other variants generally less than about 150 amino acids can be generated by synthetic means, using techniques well known to those of ordinary skill in the art. In one illustrative example, such polypeptides are synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a  
25 growing amino acid chain. *See Merrifield, J. Am. Chem. Soc.* 85:2149-2146, 1963. Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Perkin Elmer/Applied BioSystems Division (Foster City, CA), and may be operated according to the manufacturer's instructions.

In general, polypeptide compositions (including fusion polypeptides) of  
30 the invention are isolated. An "isolated" polypeptide is one that is removed from its

original environment. For example, a naturally-occurring protein or polypeptide is isolated if it is separated from some or all of the coexisting materials in the natural system. Preferably, such polypeptides are also purified, *e.g.*, are at least about 90% pure, more preferably at least about 95% pure and most preferably at least about 99%  
5 pure.

### Polynucleotide Compositions

The present invention, in other aspects, provides polynucleotide compositions. The terms "DNA" and "polynucleotide" are used essentially interchangeably herein to refer to a DNA molecule that has been isolated free of total  
10 genomic DNA of a particular species. "Isolated," as used herein, means that a polynucleotide is substantially away from other coding sequences, and that the DNA molecule does not contain large portions of unrelated coding DNA, such as large chromosomal fragments or other functional genes or polypeptide coding regions. Of course, this refers to the DNA molecule as originally isolated, and does not exclude  
15 genes or coding regions later added to the segment by the hand of man.

As will be understood by those skilled in the art, the polynucleotide compositions of this invention can include genomic sequences, extra-genomic and plasmid-encoded sequences and smaller engineered gene segments that express, or may be adapted to express, proteins, polypeptides, peptides and the like. Such segments may  
20 be naturally isolated, or modified synthetically by the hand of man.

As will be also recognized by the skilled artisan, polynucleotides of the invention may be single-stranded (coding or antisense) or double-stranded, and may be DNA (genomic, cDNA or synthetic) or RNA molecules. RNA molecules may include HnRNA molecules, which contain introns and correspond to a DNA molecule in a one-  
25 to-one manner, and mRNA molecules, which do not contain introns. Additional coding or non-coding sequences may, but need not, be present within a polynucleotide of the present invention, and a polynucleotide may, but need not, be linked to other molecules and/or support materials.

Polynucleotides may comprise a native sequence (*i.e.*, an endogenous sequence that encodes a polypeptide/protein of the invention or a portion thereof) or may comprise a sequence that encodes a variant or derivative, preferably an immunogenic variant or derivative, of such a sequence.

5           Therefore, according to another aspect of the present invention, polynucleotide compositions are provided that comprise some or all of a polynucleotide sequence set forth in any one of SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942, complements of a polynucleotide sequence set forth in any one of SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942, and degenerate variants of a polynucleotide sequence set forth in any one of SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942. In certain preferred  
15           embodiments, the polynucleotide sequences set forth herein encode immunogenic polypeptides, as described above.

          In other related embodiments, the present invention provides polynucleotide variants having substantial identity to the sequences disclosed herein in SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942, for example those comprising at least 70% sequence identity, preferably at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% or higher, sequence identity compared to a polynucleotide sequence of this  
25           invention using the methods described herein, (*e.g.*, BLAST analysis using standard  
30

parameters, as described below). One skilled in this art will recognize that these values can be appropriately adjusted to determine corresponding identity of proteins encoded by two nucleotide sequences by taking into account codon degeneracy, amino acid similarity, reading frame positioning and the like.

5           Typically, polynucleotide variants will contain one or more substitutions, additions, deletions and/or insertions, preferably such that the immunogenicity of the polypeptide encoded by the variant polynucleotide is not substantially diminished relative to a polypeptide encoded by a polynucleotide sequence specifically set forth herein). The term "variants" should also be understood to encompass homologous  
10 genes of xenogenic origin.

          In additional embodiments, the present invention provides polynucleotide fragments comprising various lengths of contiguous stretches of sequence identical to, or complementary to, one or more of the sequences disclosed herein. For example, polynucleotides are provided by this invention that comprise at  
15 least about 10, 15, 20, 30, 40, 50, 75, 100, 150, 200, 300, 400, 500 or 1000 or more contiguous nucleotides of one or more of the sequences disclosed herein as well as all intermediate lengths there between. It will be readily understood that "intermediate lengths", in this context, means any length between the quoted values, such as 16, 17, 18, 19, *etc.*; 21, 22, 23, *etc.*; 30, 31, 32, *etc.*; 50, 51, 52, 53, *etc.*; 100, 101, 102, 103,  
20 *etc.*; 150, 151, 152, 153, *etc.*; including all integers through 200-500; 500-1,000, and the like.

          In another embodiment of the invention, polynucleotide compositions are provided that are capable of hybridizing under moderate to high stringency conditions to a polynucleotide sequence provided herein, or a fragment thereof, or a complementary  
25 sequence thereof. Hybridization techniques are well known in the art of molecular biology. For purposes of illustration, suitable moderately stringent conditions for testing the hybridization of a polynucleotide of this invention with other polynucleotides include prewashing in a solution of 5 X SSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-60°C, 5 X SSC, overnight; followed by washing twice at 65°C for  
30 20 minutes with each of 2X, 0.5X and 0.2X SSC containing 0.1% SDS. One skilled in

the art will understand that the stringency of hybridization can be readily manipulated, such as by altering the salt content of the hybridization solution and/or the temperature at which the hybridization is performed. For example, in another embodiment, suitable highly stringent hybridization conditions include those described above, with the exception that the temperature of hybridization is increased, *e.g.*, to 60-65°C or 65-70°C.

In certain preferred embodiments, the polynucleotides described above, *e.g.*, polynucleotide variants, fragments and hybridizing sequences, encode polypeptides that are immunologically cross-reactive with a polypeptide sequence specifically set forth herein. In other preferred embodiments, such polynucleotides encode polypeptides that have a level of immunogenic activity of at least about 50%, preferably at least about 70%, and more preferably at least about 90% of that for a polypeptide sequence specifically set forth herein.

The polynucleotides of the present invention, or fragments thereof, regardless of the length of the coding sequence itself, may be combined with other DNA sequences, such as promoters, polyadenylation signals, additional restriction enzyme sites, multiple cloning sites, other coding segments, and the like, such that their overall length may vary considerably. It is therefore contemplated that a nucleic acid fragment of almost any length may be employed, with the total length preferably being limited by the ease of preparation and use in the intended recombinant DNA protocol. For example, illustrative polynucleotide segments with total lengths of about 10,000, about 5000, about 3000, about 2,000, about 1,000, about 500, about 200, about 100, about 50 base pairs in length, and the like, (including all intermediate lengths) are contemplated to be useful in many implementations of this invention.

When comparing polynucleotide sequences, two sequences are said to be "identical" if the sequence of nucleotides in the two sequences is the same when aligned for maximum correspondence, as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A "comparison window" as used herein, refers to a segment of at least about 20 contiguous positions,

usually 30 to about 75, preferably 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins – Matrices for detecting distant relationships. In Dayhoff, M.O. (ed.) *Atlas of Protein Sequence and Structure*, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenies pp. 626-645 *Methods in Enzymology* vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) *CABIOS* 5:151-153; Myers, E.W. and Muller W. (1988) *CABIOS* 4:11-17; Robinson, E.D. (1971) *Comb. Theor* 11:105; Santou, N. Nes, M. (1987) *Mol. Biol. Evol.* 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy*, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) *Proc. Natl. Acad., Sci. USA* 80:726-730.

Alternatively, optimal alignment of sequences for comparison may be conducted by the local identity algorithm of Smith and Waterman (1981) *Add. APL. Math* 2:482, by the identity alignment algorithm of Needleman and Wunsch (1970) *J. Mol. Biol.* 48:443, by the search for similarity methods of Pearson and Lipman (1988) *Proc. Natl. Acad. Sci. USA* 85: 2444, by computerized implementations of these algorithms (GAP, BESTFIT, BLAST, FASTA, and TFASTA in the Wisconsin Genetics Software Package, Genetics Computer Group (GCG), 575 Science Dr., Madison, WI), or by inspection.

One preferred example of algorithms that are suitable for determining percent sequence identity and sequence similarity are the BLAST and BLAST 2.0 algorithms, which are described in Altschul et al. (1977) *Nucl. Acids Res.* 25:3389-3402 and Altschul et al. (1990) *J. Mol. Biol.* 215:403-410, respectively. BLAST and BLAST 2.0 can be used, for example with the parameters described herein, to determine percent

sequence identity for the polynucleotides of the invention. Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information. In one illustrative example, cumulative scores can be calculated using, for nucleotide sequences, the parameters M (reward score for a pair of matching residues; always >0) and N (penalty score for mismatching residues; always <0). Extension of the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters W, T and X determine the sensitivity and speed of the alignment. The BLASTN program (for nucleotide sequences) uses as defaults a wordlength (W) of 11, and expectation (E) of 10, and the BLOSUM62 scoring matrix (see Henikoff and Henikoff (1989) *Proc. Natl. Acad. Sci. USA* 89:10915) alignments, (B) of 50, expectation (E) of 10, M=5, N=-4 and a comparison of both strands.

Preferably, the "percentage of sequence identity" is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polynucleotide sequence in the comparison window may comprise additions or deletions (*i.e.*, gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid bases occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (*i.e.*, the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

It will be appreciated by those of ordinary skill in the art that, as a result of the degeneracy of the genetic code, there are many nucleotide sequences that encode a polypeptide as described herein. Some of these polynucleotides bear minimal homology to the nucleotide sequence of any native gene. Nonetheless, polynucleotides that vary due to differences in codon usage are specifically contemplated by the present



invention. Further, alleles of the genes comprising the polynucleotide sequences provided herein are within the scope of the present invention. Alleles are endogenous genes that are altered as a result of one or more mutations, such as deletions, additions and/or substitutions of nucleotides. The resulting mRNA and protein may, but need not, have an altered structure or function. Alleles may be identified using standard techniques (such as hybridization, amplification and/or database sequence comparison).

Therefore, in another embodiment of the invention, a mutagenesis approach, such as site-specific mutagenesis, is employed for the preparation of immunogenic variants and/or derivatives of the polypeptides described herein. By this approach, specific modifications in a polypeptide sequence can be made through mutagenesis of the underlying polynucleotides that encode them. These techniques provides a straightforward approach to prepare and test sequence variants, for example, incorporating one or more of the foregoing considerations, by introducing one or more nucleotide sequence changes into the polynucleotide.

Site-specific mutagenesis allows the production of mutants through the use of specific oligonucleotide sequences which encode the DNA sequence of the desired mutation, as well as a sufficient number of adjacent nucleotides, to provide a primer sequence of sufficient size and sequence complexity to form a stable duplex on both sides of the deletion junction being traversed. Mutations may be employed in a selected polynucleotide sequence to improve, alter, decrease, modify, or otherwise change the properties of the polynucleotide itself, and/or alter the properties, activity, composition, stability, or primary sequence of the encoded polypeptide.

In certain embodiments of the present invention, the inventors contemplate the mutagenesis of the disclosed polynucleotide sequences to alter one or more properties of the encoded polypeptide, such as the immunogenicity of a polypeptide vaccine. The techniques of site-specific mutagenesis are well-known in the art, and are widely used to create variants of both polypeptides and polynucleotides. For example, site-specific mutagenesis is often used to alter a specific portion of a DNA molecule. In such embodiments, a primer comprising typically about 14 to about 25

nucleotides or so in length is employed, with about 5 to about 10 residues on both sides of the junction of the sequence being altered.

As will be appreciated by those of skill in the art, site-specific mutagenesis techniques have often employed a phage vector that exists in both a single stranded and double stranded form. Typical vectors useful in site-directed mutagenesis include vectors such as the M13 phage. These phage are readily commercially-available and their use is generally well-known to those skilled in the art. Double-stranded plasmids are also routinely employed in site directed mutagenesis that eliminates the step of transferring the gene of interest from a plasmid to a phage.

In general, site-directed mutagenesis in accordance herewith is performed by first obtaining a single-stranded vector or melting apart of two strands of a double-stranded vector that includes within its sequence a DNA sequence that encodes the desired peptide. An oligonucleotide primer bearing the desired mutated sequence is prepared, generally synthetically. This primer is then annealed with the single-stranded vector, and subjected to DNA polymerizing enzymes such as *E. coli* polymerase I Klenow fragment, in order to complete the synthesis of the mutation-bearing strand. Thus, a heteroduplex is formed wherein one strand encodes the original non-mutated sequence and the second strand bears the desired mutation. This heteroduplex vector is then used to transform appropriate cells, such as *E. coli* cells, and clones are selected which include recombinant vectors bearing the mutated sequence arrangement.

The preparation of sequence variants of the selected peptide-encoding DNA segments using site-directed mutagenesis provides a means of producing potentially useful species and is not meant to be limiting as there are other ways in which sequence variants of peptides and the DNA sequences encoding them may be obtained. For example, recombinant vectors encoding the desired peptide sequence may be treated with mutagenic agents, such as hydroxylamine, to obtain sequence variants. Specific details regarding these methods and protocols are found in the teachings of Maloy *et al.*, 1994; Segal, 1976; Prokop and Bajpai, 1991; Kuby, 1994; and Maniatis *et al.*, 1982, each incorporated herein by reference, for that purpose.

As used herein, the term "oligonucleotide directed mutagenesis procedure" refers to template-dependent processes and vector-mediated propagation which result in an increase in the concentration of a specific nucleic acid molecule relative to its initial concentration, or in an increase in the concentration of a detectable  
5 signal, such as amplification. As used herein, the term "oligonucleotide directed mutagenesis procedure" is intended to refer to a process that involves the template-dependent extension of a primer molecule. The term template dependent process refers to nucleic acid synthesis of an RNA or a DNA molecule wherein the sequence of the newly synthesized strand of nucleic acid is dictated by the well-known  
10 rules of complementary base pairing (see, for example, Watson, 1987). Typically, vector mediated methodologies involve the introduction of the nucleic acid fragment into a DNA or RNA vector, the clonal amplification of the vector, and the recovery of the amplified nucleic acid fragment. Examples of such methodologies are provided by U. S. Patent No. 4,237,224, specifically incorporated herein by reference in its entirety.

15 In another approach for the production of polypeptide variants of the present invention, recursive sequence recombination, as described in U.S. Patent No. 5,837,458, may be employed. In this approach, iterative cycles of recombination and screening or selection are performed to "evolve" individual polynucleotide variants of the invention having, for example, enhanced immunogenic activity.

20 In other embodiments of the present invention, the polynucleotide sequences provided herein can be advantageously used as probes or primers for nucleic acid hybridization. As such, it is contemplated that nucleic acid segments that comprise a sequence region of at least about 15 contiguous nucleotides that has the same sequence as, or is complementary to, a 15 nucleotide long contiguous sequence  
25 disclosed herein will find particular utility. Longer contiguous identical or complementary sequences, *e.g.*, those of about 20, 30, 40, 50, 100, 200, 500, 1000 (including all intermediate lengths) and even up to full length sequences will also be of use in certain embodiments.

The ability of such nucleic acid probes to specifically hybridize to a  
30 sequence of interest will enable them to be of use in detecting the presence of

complementary sequences in a given sample. However, other uses are also envisioned, such as the use of the sequence information for the preparation of mutant species primers, or primers for use in preparing other genetic constructions.

Polynucleotide molecules having sequence regions consisting of  
5 contiguous nucleotide stretches of 10-14, 15-20, 30, 50, or even of 100-200 nucleotides or so (including intermediate lengths as well), identical or complementary to a polynucleotide sequence disclosed herein, are particularly contemplated as hybridization probes for use in, *e.g.*, Southern and Northern blotting. This would allow a gene product, or fragment thereof, to be analyzed, both in diverse cell types and also in  
10 various bacterial cells. The total size of fragment, as well as the size of the complementary stretch(es), will ultimately depend on the intended use or application of the particular nucleic acid segment. Smaller fragments will generally find use in hybridization embodiments, wherein the length of the contiguous complementary region may be varied, such as between about 15 and about 100 nucleotides, but larger  
15 contiguous complementarity stretches may be used, according to the length complementary sequences one wishes to detect.

The use of a hybridization probe of about 15-25 nucleotides in length allows the formation of a duplex molecule that is both stable and selective. Molecules having contiguous complementary sequences over stretches greater than 15 bases in  
20 length are generally preferred, though, in order to increase stability and selectivity of the hybrid, and thereby improve the quality and degree of specific hybrid molecules obtained. One will generally prefer to design nucleic acid molecules having gene-complementary stretches of 15 to 25 contiguous nucleotides, or even longer where desired.

25 Hybridization probes may be selected from any portion of any of the sequences disclosed herein. All that is required is to review the sequences set forth herein, or to any continuous portion of the sequences, from about 15-25 nucleotides in length up to and including the full length sequence, that one wishes to utilize as a probe or primer. The choice of probe and primer sequences may be governed by various

factors. For example, one may wish to employ primers from towards the termini of the total sequence.

Small polynucleotide segments or fragments may be readily prepared by, for example, directly synthesizing the fragment by chemical means, as is commonly practiced using an automated oligonucleotide synthesizer. Also, fragments may be obtained by application of nucleic acid reproduction technology, such as the PCR™ technology of U. S. Patent 4,683,202 (incorporated herein by reference), by introducing selected sequences into recombinant vectors for recombinant production, and by other recombinant DNA techniques generally known to those of skill in the art of molecular biology.

The nucleotide sequences of the invention may be used for their ability to selectively form duplex molecules with complementary stretches of the entire gene or gene fragments of interest. Depending on the application envisioned, one will typically desire to employ varying conditions of hybridization to achieve varying degrees of selectivity of probe towards target sequence. For applications requiring high selectivity, one will typically desire to employ relatively stringent conditions to form the hybrids, *e.g.*, one will select relatively low salt and/or high temperature conditions, such as provided by a salt concentration of from about 0.02 M to about 0.15 M salt at temperatures of from about 50°C to about 70°C. Such selective conditions tolerate little, if any, mismatch between the probe and the template or target strand, and would be particularly suitable for isolating related sequences.

Of course, for some applications, for example, where one desires to prepare mutants employing a mutant primer strand hybridized to an underlying template, less stringent (reduced stringency) hybridization conditions will typically be needed in order to allow formation of the heteroduplex. In these circumstances, one may desire to employ salt conditions such as those of from about 0.15 M to about 0.9 M salt, at temperatures ranging from about 20°C to about 55°C. Cross-hybridizing species can thereby be readily identified as positively hybridizing signals with respect to control hybridizations. In any case, it is generally appreciated that conditions can be rendered more stringent by the addition of increasing amounts of formamide, which serves to

destabilize the hybrid duplex in the same manner as increased temperature. Thus, hybridization conditions can be readily manipulated, and thus will generally be a method of choice depending on the desired results.

According to another embodiment of the present invention, 5 polynucleotide compositions comprising antisense oligonucleotides are provided. Antisense oligonucleotides have been demonstrated to be effective and targeted inhibitors of protein synthesis, and, consequently, provide a therapeutic approach by which a disease can be treated by inhibiting the synthesis of proteins that contribute to the disease. The efficacy of antisense oligonucleotides for inhibiting protein synthesis 10 is well established. For example, the synthesis of polygalacturonase and the muscarine type 2 acetylcholine receptor are inhibited by antisense oligonucleotides directed to their respective mRNA sequences (U. S. Patent 5,739,119 and U. S. Patent 5,759,829). Further, examples of antisense inhibition have been demonstrated with the nuclear protein cyclin, the multiple drug resistance gene (MDG1), ICAM-1, E-selectin, STK-1, 15 striatal GABA<sub>A</sub> receptor and human EGF (Jaskulski *et al.*, Science. 1988 Jun 10;240(4858):1544-6; Vasanthakumar and Ahmed, Cancer Commun. 1989;1(4):225-32; Peris *et al.*, Brain Res Mol Brain Res. 1998 Jun 15;57(2):310-20; U. S. Patent 5,801,154; U.S. Patent 5,789,573; U. S. Patent 5,718,709 and U.S. Patent 5,610,288). Antisense constructs have also been described that inhibit and can be used to treat a 20 variety of abnormal cellular proliferations, *e.g.* cancer (U. S. Patent 5,747,470; U. S. Patent 5,591,317 and U. S. Patent 5,783,683).

Therefore, in certain embodiments, the present invention provides oligonucleotide sequences that comprise all, or a portion of, any sequence that is capable of specifically binding to polynucleotide sequence described herein, or a 25 complement thereof. In one embodiment, the antisense oligonucleotides comprise DNA or derivatives thereof. In another embodiment, the oligonucleotides comprise RNA or derivatives thereof. In a third embodiment, the oligonucleotides are modified DNAs comprising a phosphorothioated modified backbone. In a fourth embodiment, the oligonucleotide sequences comprise peptide nucleic acids or derivatives thereof. In 30 each case, preferred compositions comprise a sequence region that is complementary,

and more preferably substantially-complementary, and even more preferably, completely complementary to one or more portions of polynucleotides disclosed herein. Selection of antisense compositions specific for a given gene sequence is based upon analysis of the chosen target sequence and determination of secondary structure,  $T_m$ , binding energy, and relative stability. Antisense compositions may be selected based upon their relative inability to form dimers, hairpins, or other secondary structures that would reduce or prohibit specific binding to the target mRNA in a host cell. Highly preferred target regions of the mRNA, are those which are at or near the AUG translation initiation codon, and those sequences which are substantially complementary to 5' regions of the mRNA. These secondary structure analyses and target site selection considerations can be performed, for example, using v.4 of the OLIGO primer analysis software and/or the BLASTN 2.0.5 algorithm software (Altschul *et al.*, Nucleic Acids Res. 1997 Sep 1;25(17):3389-402).

The use of an antisense delivery method employing a short peptide vector, termed MPG (27 residues), is also contemplated. The MPG peptide contains a hydrophobic domain derived from the fusion sequence of HIV gp41 and a hydrophilic domain from the nuclear localization sequence of SV40 T-antigen (Morris *et al.*, Nucleic Acids Res. 1997 Jul 15;25(14):2730-6). It has been demonstrated that several molecules of the MPG peptide coat the antisense oligonucleotides and can be delivered into cultured mammalian cells in less than 1 hour with relatively high efficiency (90%). Further, the interaction with MPG strongly increases both the stability of the oligonucleotide to nuclease and the ability to cross the plasma membrane.

According to another embodiment of the invention, the polynucleotide compositions described herein are used in the design and preparation of ribozyme molecules for inhibiting expression of the tumor polypeptides and proteins of the present invention in tumor cells. Ribozymes are RNA-protein complexes that cleave nucleic acids in a site-specific fashion. Ribozymes have specific catalytic domains that possess endonuclease activity (Kim and Cech, Proc Natl Acad Sci U S A. 1987 Dec;84(24):8788-92; Forster and Symons, Cell. 1987 Apr 24;49(2):211-20). For example, a large number of ribozymes accelerate phosphoester transfer reactions with a

high degree of specificity, often cleaving only one of several phosphoesters in an oligonucleotide substrate (Cech *et al.*, Cell. 1981 Dec;27(3 Pt 2):487-96; Michel and Westhof, J Mol Biol. 1990 Dec 5;216(3):585-610; Reinhold-Hurek and Shub, Nature. 1992 May 14;357(6374):173-6). This specificity has been attributed to the requirement  
5 that the substrate bind via specific base-pairing interactions to the internal guide sequence ("IGS") of the ribozyme prior to chemical reaction.

Six basic varieties of naturally-occurring enzymatic RNAs are known presently. Each can catalyze the hydrolysis of RNA phosphodiester bonds *in trans* (and thus can cleave other RNA molecules) under physiological conditions. In general,  
10 enzymatic nucleic acids act by first binding to a target RNA. Such binding occurs through the target binding portion of a enzymatic nucleic acid which is held in close proximity to an enzymatic portion of the molecule that acts to cleave the target RNA. Thus, the enzymatic nucleic acid first recognizes and then binds a target RNA through complementary base-pairing, and once bound to the correct site, acts enzymatically to  
15 cut the target RNA. Strategic cleavage of such a target RNA will destroy its ability to direct synthesis of an encoded protein. After an enzymatic nucleic acid has bound and cleaved its RNA target, it is released from that RNA to search for another target and can repeatedly bind and cleave new targets.

The enzymatic nature of a ribozyme is advantageous over many  
20 technologies, such as antisense technology (where a nucleic acid molecule simply binds to a nucleic acid target to block its translation) since the concentration of ribozyme necessary to affect a therapeutic treatment is lower than that of an antisense oligonucleotide. This advantage reflects the ability of the ribozyme to act enzymatically. Thus, a single ribozyme molecule is able to cleave many molecules of  
25 target RNA. In addition, the ribozyme is a highly specific inhibitor, with the specificity of inhibition depending not only on the base pairing mechanism of binding to the target RNA, but also on the mechanism of target RNA cleavage. Single mismatches, or base-substitutions, near the site of cleavage can completely eliminate catalytic activity of a ribozyme. Similar mismatches in antisense molecules do not prevent their action  
30 (Woolf *et al.*, Proc Natl Acad Sci U S A. 1992 Aug 15;89(16):7305-9). Thus, the



specificity of action of a ribozyme is greater than that of an antisense oligonucleotide binding the same RNA site.

The enzymatic nucleic acid molecule may be formed in a hammerhead, hairpin, a hepatitis  $\delta$  virus, group I intron or RNaseP RNA (in association with an RNA guide sequence) or Neurospora VS RNA motif. Examples of hammerhead motifs are described by Rossi *et al.* Nucleic Acids Res. 1992 Sep 11;20(17):4559-65. Examples of hairpin motifs are described by Hampel *et al.* (Eur. Pat. Appl. Publ. No. EP 0360257), Hampel and Tritz, Biochemistry 1989 Jun 13;28(12):4929-33; Hampel *et al.*, Nucleic Acids Res. 1990 Jan 25;18(2):299-304 and U. S. Patent 5,631,359. An example of the hepatitis  $\delta$  virus motif is described by Perrotta and Been, Biochemistry. 1992 Dec 1;31(47):11843-52; an example of the RNaseP motif is described by Guerrier-Takada *et al.*, Cell. 1983 Dec;35(3 Pt 2):849-57; Neurospora VS RNA ribozyme motif is described by Collins (Saville and Collins, Cell. 1990 May 18;61(4):685-96; Saville and Collins, Proc Natl Acad Sci U S A. 1991 Oct 1;88(19):8826-30; Collins and Olive, Biochemistry. 1993 Mar 23;32(11):2795-9); and an example of the Group I intron is described in (U. S. Patent 4,987,071). All that is important in an enzymatic nucleic acid molecule of this invention is that it has a specific substrate binding site which is complementary to one or more of the target gene RNA regions, and that it have nucleotide sequences within or surrounding that substrate binding site which impart an RNA cleaving activity to the molecule. Thus the ribozyme constructs need not be limited to specific motifs mentioned herein.

Ribozymes may be designed as described in Int. Pat. Appl. Publ. No. WO 93/23569 and Int. Pat. Appl. Publ. No. WO 94/02595, each specifically incorporated herein by reference) and synthesized to be tested *in vitro* and *in vivo*, as described. Such ribozymes can also be optimized for delivery. While specific examples are provided, those in the art will recognize that equivalent RNA targets in other species can be utilized when necessary.

Ribozyme activity can be optimized by altering the length of the ribozyme binding arms, or chemically synthesizing ribozymes with modifications that prevent their degradation by serum ribonucleases (see *e.g.*, Int. Pat. Appl. Publ. No. WO

92/07065; Int. Pat. Appl. Publ. No. WO 93/15187; Int. Pat. Appl. Publ. No. WO 91/03162; Eur. Pat. Appl. Publ. No. 92110298.4; U. S. Patent 5,334,711; and Int. Pat. Appl. Publ. No. WO 94/13688, which describe various chemical modifications that can be made to the sugar moieties of enzymatic RNA molecules), modifications which enhance their efficacy in cells, and removal of stem II bases to shorten RNA synthesis times and reduce chemical requirements.

Sullivan *et al.* (Int. Pat. Appl. Publ. No. WO 94/02595) describes the general methods for delivery of enzymatic RNA molecules. Ribozymes may be administered to cells by a variety of methods known to those familiar to the art, including, but not restricted to, encapsulation in liposomes, by iontophoresis, or by incorporation into other vehicles, such as hydrogels, cyclodextrins, biodegradable nanocapsules, and bioadhesive microspheres. For some indications, ribozymes may be directly delivered *ex vivo* to cells or tissues with or without the aforementioned vehicles. Alternatively, the RNA/vehicle combination may be locally delivered by direct inhalation, by direct injection or by use of a catheter, infusion pump or stent. Other routes of delivery include, but are not limited to, intravascular, intramuscular, subcutaneous or joint injection, aerosol inhalation, oral (tablet or pill form), topical, systemic, ocular, intraperitoneal and/or intrathecal delivery. More detailed descriptions of ribozyme delivery and administration are provided in Int. Pat. Appl. Publ. No. WO 94/02595 and Int. Pat. Appl. Publ. No. WO 93/23569, each specifically incorporated herein by reference.

Another means of accumulating high concentrations of a ribozyme(s) within cells is to incorporate the ribozyme-encoding sequences into a DNA expression vector. Transcription of the ribozyme sequences are driven from a promoter for eukaryotic RNA polymerase I (pol I), RNA polymerase II (pol II), or RNA polymerase III (pol III). Transcripts from pol II or pol III promoters will be expressed at high levels in all cells; the levels of a given pol II promoter in a given cell type will depend on the nature of the gene regulatory sequences (enhancers, silencers, *etc.*) present nearby. Prokaryotic RNA polymerase promoters may also be used, providing that the prokaryotic RNA polymerase enzyme is expressed in the appropriate cells. Ribozymes

expressed from such promoters have been shown to function in mammalian cells. Such transcription units can be incorporated into a variety of vectors for introduction into mammalian cells, including but not restricted to, plasmid DNA vectors, viral DNA vectors (such as adenovirus or adeno-associated vectors), or viral RNA vectors (such as retroviral, semliki forest virus, sindbis virus vectors).

In another embodiment of the invention, peptide nucleic acids (PNAs) compositions are provided. PNA is a DNA mimic in which the nucleobases are attached to a pseudopeptide backbone (Good and Nielsen, *Antisense Nucleic Acid Drug Dev.* 1997 7(4) 431-37). PNA is able to be utilized in a number methods that traditionally have used RNA or DNA. Often PNA sequences perform better in techniques than the corresponding RNA or DNA sequences and have utilities that are not inherent to RNA or DNA. A review of PNA including methods of making, characteristics of, and methods of using, is provided by Corey (*Trends Biotechnol* 1997 Jun;15(6):224-9). As such, in certain embodiments, one may prepare PNA sequences that are complementary to one or more portions of the ACE mRNA sequence, and such PNA compositions may be used to regulate, alter, decrease, or reduce the translation of ACE-specific mRNA, and thereby alter the level of ACE activity in a host cell to which such PNA compositions have been administered.

PNAs have 2-aminoethyl-glycine linkages replacing the normal phosphodiester backbone of DNA (Nielsen *et al.*, *Science* 1991 Dec 6;254(5037):1497-500; Hanvey *et al.*, *Science*. 1992 Nov 27;258(5087):1481-5; Hyrup and Nielsen, *Bioorg Med Chem.* 1996 Jan;4(1):5-23). This chemistry has three important consequences: firstly, in contrast to DNA or phosphorothioate oligonucleotides, PNAs are neutral molecules; secondly, PNAs are achiral, which avoids the need to develop a stereoselective synthesis; and thirdly, PNA synthesis uses standard Boc or Fmoc protocols for solid-phase peptide synthesis, although other methods, including a modified Merrifield method, have been used.

PNA monomers or ready-made oligomers are commercially available from PerSeptive Biosystems (Framingham, MA). PNA syntheses by either Boc or Fmoc protocols are straightforward using manual or automated protocols (Norton *et al.*,

Bioorg Med Chem. 1995 Apr;3(4):437-45). The manual protocol lends itself to the production of chemically modified PNAs or the simultaneous synthesis of families of closely related PNAs.

As with peptide synthesis, the success of a particular PNA synthesis will  
5 depend on the properties of the chosen sequence. For example, while in theory PNAs can incorporate any combination of nucleotide bases, the presence of adjacent purines can lead to deletions of one or more residues in the product. In expectation of this difficulty, it is suggested that, in producing PNAs with adjacent purines, one should repeat the coupling of residues likely to be added inefficiently. This should be followed  
10 by the purification of PNAs by reverse-phase high-pressure liquid chromatography, providing yields and purity of product similar to those observed during the synthesis of peptides.

Modifications of PNAs for a given application may be accomplished by coupling amino acids during solid-phase synthesis or by attaching compounds that  
15 contain a carboxylic acid group to the exposed N-terminal amine. Alternatively, PNAs can be modified after synthesis by coupling to an introduced lysine or cysteine. The ease with which PNAs can be modified facilitates optimization for better solubility or for specific functional requirements. Once synthesized, the identity of PNAs and their derivatives can be confirmed by mass spectrometry. Several studies have made and  
20 utilized modifications of PNAs (for example, Norton *et al.*, Bioorg Med Chem. 1995 Apr;3(4):437-45; Petersen *et al.*, J Pept Sci. 1995 May-Jun;1(3):175-83; Orum *et al.*, Biotechniques. 1995 Sep;19(3):472-80; Footer *et al.*, Biochemistry. 1996 Aug 20;35(33):10673-9; Griffith *et al.*, Nucleic Acids Res. 1995 Aug 11;23(15):3003-8; Pardridge *et al.*, Proc Natl Acad Sci U S A. 1995 Jun 6;92(12):5592-6; Boffa *et al.*,  
25 Proc Natl Acad Sci U S A. 1995 Mar 14;92(6):1901-5; Gambacorti-Passerini *et al.*, Blood. 1996 Aug 15;88(4):1411-7; Armitage *et al.*, Proc Natl Acad Sci U S A. 1997 Nov 11;94(23):12320-5; Seeger *et al.*, Biotechniques. 1997 Sep;23(3):512-7). U.S. Patent No. 5,700,922 discusses PNA-DNA-PNA chimeric molecules and their uses in diagnostics, modulating protein in organisms, and treatment of conditions susceptible to  
30 therapeutics.

Methods of characterizing the antisense binding properties of PNAs are discussed in Rose (Anal Chem. 1993 Dec 15;65(24):3545-9) and Jensen *et al.* (Biochemistry. 1997 Apr 22;36(16):5072-7). Rose uses capillary gel electrophoresis to determine binding of PNAs to their complementary oligonucleotide, measuring the relative binding kinetics and stoichiometry. Similar types of measurements were made by Jensen *et al.* using BIAcore™ technology.

Other applications of PNAs that have been described and will be apparent to the skilled artisan include use in DNA strand invasion, antisense inhibition, mutational analysis, enhancers of transcription, nucleic acid purification, isolation of transcriptionally active genes, blocking of transcription factor binding, genome cleavage, biosensors, *in situ* hybridization, and the like.

#### Polynucleotide Identification, Characterization and Expression

Polynucleotide compositions of the present invention may be identified, prepared and/or manipulated using any of a variety of well established techniques (see generally, Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989, and other like references). For example, a polynucleotide may be identified, as described in more detail below, by screening a microarray of cDNAs for tumor-associated expression (*i.e.*, expression that is at least two fold greater in a tumor than in normal tissue, as determined using a representative assay provided herein). Such screens may be performed, for example, using the microarray technology of Affymetrix, Inc. (Santa Clara, CA) according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA* 93:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA* 94:2150-2155, 1997). Alternatively, polynucleotides may be amplified from cDNA prepared from cells expressing the proteins described herein, such as tumor cells.

Many template dependent processes are available to amplify a target sequences of interest present in a sample. One of the best known amplification methods is the polymerase chain reaction (PCR™) which is described in detail in U.S. Patent Nos. 4,683,195, 4,683,202 and 4,800,159, each of which is incorporated herein by

reference in its entirety. Briefly, in PCR<sup>TM</sup>, two primer sequences are prepared which are complementary to regions on opposite complementary strands of the target sequence. An excess of deoxynucleoside triphosphates is added to a reaction mixture along with a DNA polymerase (*e.g.*, *Taq* polymerase). If the target sequence is present  
5 in a sample, the primers will bind to the target and the polymerase will cause the primers to be extended along the target sequence by adding on nucleotides. By raising and lowering the temperature of the reaction mixture, the extended primers will dissociate from the target to form reaction products, excess primers will bind to the target and to the reaction product and the process is repeated. Preferably reverse  
10 transcription and PCR<sup>TM</sup> amplification procedure may be performed in order to quantify the amount of mRNA amplified. Polymerase chain reaction methodologies are well known in the art.

Any of a number of other template dependent processes, many of which are variations of the PCR<sup>TM</sup> amplification technique, are readily known and available in  
15 the art. Illustratively, some such methods include the ligase chain reaction (referred to as LCR), described, for example, in Eur. Pat. Appl. Publ. No. 320,308 and U.S. Patent No. 4,883,750; Qbeta Replicase, described in PCT Intl. Pat. Appl. Publ. No. PCT/US87/00880; Strand Displacement Amplification (SDA) and Repair Chain Reaction (RCR). Still other amplification methods are described in Great Britain Pat.  
20 Appl. No. 2 202 328, and in PCT Intl. Pat. Appl. Publ. No. PCT/US89/01025. Other nucleic acid amplification procedures include transcription-based amplification systems (TAS) (PCT Intl. Pat. Appl. Publ. No. WO 88/10315), including nucleic acid sequence based amplification (NASBA) and 3SR. Eur. Pat. Appl. Publ. No. 329,822 describes a nucleic acid amplification process involving cyclically synthesizing single-stranded  
25 RNA ("ssRNA"), ssDNA, and double-stranded DNA (dsDNA). PCT Intl. Pat. Appl. Publ. No. WO 89/06700 describes a nucleic acid sequence amplification scheme based on the hybridization of a promoter/primer sequence to a target single-stranded DNA ("ssDNA") followed by transcription of many RNA copies of the sequence. Other amplification methods such as "RACE" (Frohman, 1990), and "one-sided PCR" (Ohara,  
30 1989) are also well-known to those of skill in the art.

An amplified portion of a polynucleotide of the present invention may be used to isolate a full length gene from a suitable library (*e.g.*, a tumor cDNA library) using well known techniques. Within such techniques, a library (cDNA or genomic) is screened using one or more polynucleotide probes or primers suitable for amplification.

- 5 Preferably, a library is size-selected to include larger molecules. Random primed libraries may also be preferred for identifying 5' and upstream regions of genes. Genomic libraries are preferred for obtaining introns and extending 5' sequences.

- For hybridization techniques, a partial sequence may be labeled (*e.g.*, by nick-translation or end-labeling with  $^{32}\text{P}$ ) using well known techniques. A bacterial or  
10 bacteriophage library is then generally screened by hybridizing filters containing denatured bacterial colonies (or lawns containing phage plaques) with the labeled probe (*see* Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989). Hybridizing colonies or plaques are selected and expanded, and the DNA is isolated for further analysis. cDNA clones may  
15 be analyzed to determine the amount of additional sequence by, for example, PCR using a primer from the partial sequence and a primer from the vector. Restriction maps and partial sequences may be generated to identify one or more overlapping clones. The complete sequence may then be determined using standard techniques, which may involve generating a series of deletion clones. The resulting overlapping sequences can  
20 then assembled into a single contiguous sequence. A full length cDNA molecule can be generated by ligating suitable fragments, using well known techniques.

- Alternatively, amplification techniques, such as those described above, can be useful for obtaining a full length coding sequence from a partial cDNA sequence. One such amplification technique is inverse PCR (*see* Triglia et al., *Nucl. Acids Res.*  
25 16:8186, 1988), which uses restriction enzymes to generate a fragment in the known region of the gene. The fragment is then circularized by intramolecular ligation and used as a template for PCR with divergent primers derived from the known region. Within an alternative approach, sequences adjacent to a partial sequence may be retrieved by amplification with a primer to a linker sequence and a primer specific to a  
30 known region. The amplified sequences are typically subjected to a second round of

amplification with the same linker primer and a second primer specific to the known region. A variation on this procedure, which employs two primers that initiate extension in opposite directions from the known sequence, is described in WO 96/38591. Another such technique is known as "rapid amplification of cDNA ends" or RACE. This technique involves the use of an internal primer and an external primer, which hybridizes to a polyA region or vector sequence, to identify sequences that are 5' and 3' of a known sequence. Additional techniques include capture PCR (Lagerstrom et al., *PCR Methods Applic.* 1:111-19, 1991) and walking PCR (Parker et al., *Nucl. Acids. Res.* 19:3055-60, 1991). Other methods employing amplification may also be employed to obtain a full length cDNA sequence.

In certain instances, it is possible to obtain a full length cDNA sequence by analysis of sequences provided in an expressed sequence tag (EST) database, such as that available from GenBank. Searches for overlapping ESTs may generally be performed using well known programs (*e.g.*, NCBI BLAST searches), and such ESTs may be used to generate a contiguous full length sequence. Full length DNA sequences may also be obtained by analysis of genomic fragments.

In other embodiments of the invention, polynucleotide sequences or fragments thereof which encode polypeptides of the invention, or fusion proteins or functional equivalents thereof, may be used in recombinant DNA molecules to direct expression of a polypeptide in appropriate host cells. Due to the inherent degeneracy of the genetic code, other DNA sequences that encode substantially the same or a functionally equivalent amino acid sequence may be produced and these sequences may be used to clone and express a given polypeptide.

As will be understood by those of skill in the art, it may be advantageous in some instances to produce polypeptide-encoding nucleotide sequences possessing non-naturally occurring codons. For example, codons preferred by a particular prokaryotic or eukaryotic host can be selected to increase the rate of protein expression or to produce a recombinant RNA transcript having desirable properties, such as a half-life which is longer than that of a transcript generated from the naturally occurring sequence.



Moreover, the polynucleotide sequences of the present invention can be engineered using methods generally known in the art in order to alter polypeptide encoding sequences for a variety of reasons, including but not limited to, alterations which modify the cloning, processing, and/or expression of the gene product. For example, DNA shuffling by random fragmentation and PCR reassembly of gene fragments and synthetic oligonucleotides may be used to engineer the nucleotide sequences. In addition, site-directed mutagenesis may be used to insert new restriction sites, alter glycosylation patterns, change codon preference, produce splice variants, or introduce mutations, and so forth.

In another embodiment of the invention, natural, modified, or recombinant nucleic acid sequences may be ligated to a heterologous sequence to encode a fusion protein. For example, to screen peptide libraries for inhibitors of polypeptide activity, it may be useful to encode a chimeric protein that can be recognized by a commercially available antibody. A fusion protein may also be engineered to contain a cleavage site located between the polypeptide-encoding sequence and the heterologous protein sequence, so that the polypeptide may be cleaved and purified away from the heterologous moiety.

Sequences encoding a desired polypeptide may be synthesized, in whole or in part, using chemical methods well known in the art (see Caruthers, M. H. et al. (1980) *Nucl. Acids Res. Symp. Ser.* 215-223, Horn, T. et al. (1980) *Nucl. Acids Res. Symp. Ser.* 225-232). Alternatively, the protein itself may be produced using chemical methods to synthesize the amino acid sequence of a polypeptide, or a portion thereof. For example, peptide synthesis can be performed using various solid-phase techniques (Roberge, J. Y. et al. (1995) *Science* 269:202-204) and automated synthesis may be achieved, for example, using the ABI 431A Peptide Synthesizer (Perkin Elmer, Palo Alto, CA).

A newly synthesized peptide may be substantially purified by preparative high performance liquid chromatography (*e.g.*, Creighton, T. (1983) *Proteins, Structures and Molecular Principles*, WH Freeman and Co., New York, N.Y.) or other comparable techniques available in the art. The composition of the synthetic peptides may be

confirmed by amino acid analysis or sequencing (e.g., the Edman degradation procedure). Additionally, the amino acid sequence of a polypeptide, or any part thereof, may be altered during direct synthesis and/or combined using chemical methods with sequences from other proteins, or any part thereof, to produce a variant polypeptide.

5           In order to express a desired polypeptide, the nucleotide sequences encoding the polypeptide, or functional equivalents, may be inserted into appropriate expression vector, *i.e.*, a vector which contains the necessary elements for the transcription and translation of the inserted coding sequence. Methods which are well known to those skilled in the art may be used to construct expression vectors containing  
10 sequences encoding a polypeptide of interest and appropriate transcriptional and translational control elements. These methods include *in vitro* recombinant DNA techniques, synthetic techniques, and *in vivo* genetic recombination. Such techniques are described, for example, in Sambrook, J. et al. (1989) *Molecular Cloning, A Laboratory Manual*, Cold Spring Harbor Press, Plainview, N.Y., and Ausubel, F. M. et al. (1989) *Current Protocols in Molecular Biology*, John Wiley & Sons, New York.  
15 N.Y.

A variety of expression vector/host systems may be utilized to contain and express polynucleotide sequences. These include, but are not limited to, microorganisms such as bacteria transformed with recombinant bacteriophage, plasmid,  
20 or cosmid DNA expression vectors; yeast transformed with yeast expression vectors; insect cell systems infected with virus expression vectors (e.g., baculovirus); plant cell systems transformed with virus expression vectors (e.g., cauliflower mosaic virus, CaMV; tobacco mosaic virus, TMV) or with bacterial expression vectors (e.g., Ti or pBR322 plasmids); or animal cell systems.

25           The "control elements" or "regulatory sequences" present in an expression vector are those non-translated regions of the vector--enhancers, promoters, 5' and 3' untranslated regions--which interact with host cellular proteins to carry out transcription and translation. Such elements may vary in their strength and specificity. Depending on the vector system and host utilized, any number of suitable transcription  
30 and translation elements, including constitutive and inducible promoters, may be used.

For example, when cloning in bacterial systems, inducible promoters such as the hybrid lacZ promoter of the PBLUESCRIPT phagemid (Stratagene, La Jolla, Calif.) or PSPORT1 plasmid (Gibco BRL, Gaithersburg, MD) and the like may be used. In mammalian cell systems, promoters from mammalian genes or from mammalian viruses  
5 are generally preferred. If it is necessary to generate a cell line that contains multiple copies of the sequence encoding a polypeptide, vectors based on SV40 or EBV may be advantageously used with an appropriate selectable marker.

In bacterial systems, any of a number of expression vectors may be selected depending upon the use intended for the expressed polypeptide. For example,  
10 when large quantities are needed, for example for the induction of antibodies, vectors which direct high level expression of fusion proteins that are readily purified may be used. Such vectors include, but are not limited to, the multifunctional *E. coli* cloning and expression vectors such as BLUESCRIPT (Stratagene), in which the sequence encoding the polypeptide of interest may be ligated into the vector in frame with  
15 sequences for the amino-terminal Met and the subsequent 7 residues of  $\beta$ -galactosidase so that a hybrid protein is produced; pIN vectors (Van Heeke, G. and S. M. Schuster (1989) *J. Biol. Chem.* 264:5503-5509); and the like. pGEX Vectors (Promega, Madison, Wis.) may also be used to express foreign polypeptides as fusion proteins with glutathione S-transferase (GST). In general, such fusion proteins are  
20 soluble and can easily be purified from lysed cells by adsorption to glutathione-agarose beads followed by elution in the presence of free glutathione. Proteins made in such systems may be designed to include heparin, thrombin, or factor XA protease cleavage sites so that the cloned polypeptide of interest can be released from the GST moiety at will.

25 In the yeast, *Saccharomyces cerevisiae*, a number of vectors containing constitutive or inducible promoters such as alpha factor, alcohol oxidase, and PGH may be used. For reviews, see Ausubel et al. (supra) and Grant et al. (1987) *Methods Enzymol.* 153:516-544.

In cases where plant expression vectors are used, the expression of  
30 sequences encoding polypeptides may be driven by any of a number of promoters. For

example, viral promoters such as the 35S and 19S promoters of CaMV may be used alone or in combination with the omega leader sequence from TMV (Takamatsu, N. (1987) *EMBO J.* 6:307-311. Alternatively, plant promoters such as the small subunit of RUBISCO or heat shock promoters may be used (Coruzzi, G. et al. (1984) *EMBO J.* 3:1671-1680; Broglie, R. et al. (1984) *Science* 224:838-843; and Winter, J. et al. (1991) *Results Probl. Cell Differ.* 17:85-105). These constructs can be introduced into plant cells by direct DNA transformation or pathogen-mediated transfection. Such techniques are described in a number of generally available reviews (see, for example, Hobbs, S. or Murry, L. E. in McGraw Hill Yearbook of Science and Technology (1992) McGraw Hill, New York, N.Y.; pp. 191-196).

An insect system may also be used to express a polypeptide of interest. For example, in one such system, Autographa californica nuclear polyhedrosis virus (AcNPV) is used as a vector to express foreign genes in *Spodoptera frugiperda* cells or in *Trichoplusia* larvae. The sequences encoding the polypeptide may be cloned into a non-essential region of the virus, such as the polyhedrin gene, and placed under control of the polyhedrin promoter. Successful insertion of the polypeptide-encoding sequence will render the polyhedrin gene inactive and produce recombinant virus lacking coat protein. The recombinant viruses may then be used to infect, for example, *S. frugiperda* cells or *Trichoplusia* larvae in which the polypeptide of interest may be expressed (Engelhard, E. K. et al. (1994) *Proc. Natl. Acad. Sci.* 91 :3224-3227).

In mammalian host cells, a number of viral-based expression systems are generally available. For example, in cases where an adenovirus is used as an expression vector, sequences encoding a polypeptide of interest may be ligated into an adenovirus transcription/translation complex consisting of the late promoter and tripartite leader sequence. Insertion in a non-essential E1 or E3 region of the viral genome may be used to obtain a viable virus which is capable of expressing the polypeptide in infected host cells (Logan, J. and Shenk, T. (1984) *Proc. Natl. Acad. Sci.* 81:3655-3659). In addition, transcription enhancers, such as the Rous sarcoma virus (RSV) enhancer, may be used to increase expression in mammalian host cells.

Specific initiation signals may also be used to achieve more efficient translation of sequences encoding a polypeptide of interest. Such signals include the ATG initiation codon and adjacent sequences. In cases where sequences encoding the polypeptide, its initiation codon, and upstream sequences are inserted into the appropriate expression vector, no additional transcriptional or translational control signals may be needed. However, in cases where only coding sequence, or a portion thereof, is inserted, exogenous translational control signals including the ATG initiation codon should be provided. Furthermore, the initiation codon should be in the correct reading frame to ensure translation of the entire insert. Exogenous translational elements and initiation codons may be of various origins, both natural and synthetic. The efficiency of expression may be enhanced by the inclusion of enhancers which are appropriate for the particular cell system which is used, such as those described in the literature (Scharf, D. et al. (1994) *Results Probl. Cell Differ.* 20:125-162).

In addition, a host cell strain may be chosen for its ability to modulate the expression of the inserted sequences or to process the expressed protein in the desired fashion. Such modifications of the polypeptide include, but are not limited to, acetylation, carboxylation, glycosylation, phosphorylation, lipidation, and acylation. Post-translational processing which cleaves a "prepro" form of the protein may also be used to facilitate correct insertion, folding and/or function. Different host cells such as CHO, COS, HeLa, MDCK, HEK293, and WI38, which have specific cellular machinery and characteristic mechanisms for such post-translational activities, may be chosen to ensure the correct modification and processing of the foreign protein.

For long-term, high-yield production of recombinant proteins, stable expression is generally preferred. For example, cell lines which stably express a polynucleotide of interest may be transformed using expression vectors which may contain viral origins of replication and/or endogenous expression elements and a selectable marker gene on the same or on a separate vector. Following the introduction of the vector, cells may be allowed to grow for 1-2 days in an enriched media before they are switched to selective media. The purpose of the selectable marker is to confer resistance to selection, and its presence allows growth and recovery of cells which

successfully express the introduced sequences. Resistant clones of stably transformed cells may be proliferated using tissue culture techniques appropriate to the cell type.

Any number of selection systems may be used to recover transformed cell lines. These include, but are not limited to, the herpes simplex virus thymidine kinase (Wigler, M. et al. (1977) *Cell* 11:223-32) and adenine phosphoribosyltransferase (Lowy, I. et al. (1990) *Cell* 22:817-23) genes which can be employed in tk.sup.- or apt.sup.- cells, respectively. Also, antimetabolite, antibiotic or herbicide resistance can be used as the basis for selection; for example, dhfr which confers resistance to methotrexate (Wigler, M. et al. (1980) *Proc. Natl. Acad. Sci.* 77:3567-70); npt, which confers resistance to the aminoglycosides, neomycin and G-418 (Colbere-Garapin, F. et al (1981) *J. Mol. Biol.* 150:1-14); and als or pat, which confer resistance to chlorsulfuron and phosphinotricin acetyltransferase, respectively (Murry, *supra*). Additional selectable genes have been described, for example, trpB, which allows cells to utilize indole in place of tryptophan, or hisD, which allows cells to utilize histinol in place of histidine (Hartman, S. C. and R. C. Mulligan (1988) *Proc. Natl. Acad. Sci.* 85:8047-51). The use of visible markers has gained popularity with such markers as anthocyanins, beta-glucuronidase and its substrate GUS, and luciferase and its substrate luciferin, being widely used not only to identify transformants, but also to quantify the amount of transient or stable protein expression attributable to a specific vector system (Rhodes, C. A. et al. (1995) *Methods Mol. Biol.* 55:121-131).

Although the presence/absence of marker gene expression suggests that the gene of interest is also present, its presence and expression may need to be confirmed. For example, if the sequence encoding a polypeptide is inserted within a marker gene sequence, recombinant cells containing sequences can be identified by the absence of marker gene function. Alternatively, a marker gene can be placed in tandem with a polypeptide-encoding sequence under the control of a single promoter. Expression of the marker gene in response to induction or selection usually indicates expression of the tandem gene as well.

Alternatively, host cells that contain and express a desired polynucleotide sequence may be identified by a variety of procedures known to those of

skill in the art. These procedures include, but are not limited to, DNA-DNA or DNA-RNA hybridizations and protein bioassay or immunoassay techniques which include, for example, membrane, solution, or chip based technologies for the detection and/or quantification of nucleic acid or protein.

5           A variety of protocols for detecting and measuring the expression of polynucleotide-encoded products, using either polyclonal or monoclonal antibodies specific for the product are known in the art. Examples include enzyme-linked immunosorbent assay (ELISA), radioimmunoassay (RIA), and fluorescence activated cell sorting (FACS). A two-site, monoclonal-based immunoassay utilizing monoclonal  
10 antibodies reactive to two non-interfering epitopes on a given polypeptide may be preferred for some applications, but a competitive binding assay may also be employed. These and other assays are described, among other places, in Hampton, R. et al. (1990; *Serological Methods, a Laboratory Manual*, APS Press, St Paul, Minn.) and Maddox, D. E. et al. (1983; *J. Exp. Med.* 158:1211-1216).

15           A wide variety of labels and conjugation techniques are known by those skilled in the art and may be used in various nucleic acid and amino acid assays. Means for producing labeled hybridization or PCR probes for detecting sequences related to polynucleotides include oligolabeling, nick translation, end-labeling or PCR amplification using a labeled nucleotide. Alternatively, the sequences, or any portions  
20 thereof may be cloned into a vector for the production of an mRNA probe. Such vectors are known in the art, are commercially available, and may be used to synthesize RNA probes in vitro by addition of an appropriate RNA polymerase such as T7, T3, or SP6 and labeled nucleotides. These procedures may be conducted using a variety of commercially available kits. Suitable reporter molecules or labels, which may be used  
25 include radionuclides, enzymes, fluorescent, chemiluminescent, or chromogenic agents as well as substrates, cofactors, inhibitors, magnetic particles, and the like.

Host cells transformed with a polynucleotide sequence of interest may be cultured under conditions suitable for the expression and recovery of the protein from cell culture. The protein produced by a recombinant cell may be secreted or contained  
30 intracellularly depending on the sequence and/or the vector used. As will be understood

by those of skill in the art, expression vectors containing polynucleotides of the invention may be designed to contain signal sequences which direct secretion of the encoded polypeptide through a prokaryotic or eukaryotic cell membrane. Other recombinant constructions may be used to join sequences encoding a polypeptide of interest to nucleotide sequence encoding a polypeptide domain which will facilitate purification of soluble proteins. Such purification facilitating domains include, but are not limited to, metal chelating peptides such as histidine-tryptophan modules that allow purification on immobilized metals, protein A domains that allow purification on immobilized immunoglobulin, and the domain utilized in the FLAGS extension/affinity purification system (Immunex Corp., Seattle, Wash.). The inclusion of cleavable linker sequences such as those specific for Factor XA or enterokinase (Invitrogen, San Diego, Calif.) between the purification domain and the encoded polypeptide may be used to facilitate purification. One such expression vector provides for expression of a fusion protein containing a polypeptide of interest and a nucleic acid encoding 6 histidine residues preceding a thioredoxin or an enterokinase cleavage site. The histidine residues facilitate purification on IMIAC (immobilized metal ion affinity chromatography) as described in Porath, J. et al. (1992, *Prot. Exp. Purif.* 3:263-281) while the enterokinase cleavage site provides a means for purifying the desired polypeptide from the fusion protein. A discussion of vectors which contain fusion proteins is provided in Kroll, D. J. et al. (1993; *DNA Cell Biol.* 12:441-453).

In addition to recombinant production methods, polypeptides of the invention, and fragments thereof, may be produced by direct peptide synthesis using solid-phase techniques (Merrifield J. (1963) *J. Am. Chem. Soc.* 85:2149-2154). Protein synthesis may be performed using manual techniques or by automation. Automated synthesis may be achieved, for example, using Applied Biosystems 431A Peptide Synthesizer (Perkin Elmer). Alternatively, various fragments may be chemically synthesized separately and combined using chemical methods to produce the full length molecule.



Antibody Compositions, Fragments Thereof and Other Binding Agents

According to another aspect, the present invention further provides binding agents, such as antibodies and antigen-binding fragments thereof, that exhibit immunological binding to a tumor polypeptide disclosed herein, or to a portion, variant  
5 or derivative thereof. An antibody, or antigen-binding fragment thereof, is said to "specifically bind," "immunologically bind," and/or is "immunologically reactive" to a polypeptide of the invention if it reacts at a detectable level (within, for example, an ELISA assay) with the polypeptide, and does not react detectably with unrelated polypeptides under similar conditions.

10 Immunological binding, as used in this context, generally refers to the non-covalent interactions of the type which occur between an immunoglobulin molecule and an antigen for which the immunoglobulin is specific. The strength, or affinity of immunological binding interactions can be expressed in terms of the dissociation constant ( $K_d$ ) of the interaction, wherein a smaller  $K_d$  represents a greater  
15 affinity. Immunological binding properties of selected polypeptides can be quantified using methods well known in the art. One such method entails measuring the rates of antigen-binding site/antigen complex formation and dissociation, wherein those rates depend on the concentrations of the complex partners, the affinity of the interaction, and on geometric parameters that equally influence the rate in both directions. Thus, both  
20 the "on rate constant" ( $K_{on}$ ) and the "off rate constant" ( $K_{off}$ ) can be determined by calculation of the concentrations and the actual rates of association and dissociation. The ratio of  $K_{off}/K_{on}$  enables cancellation of all parameters not related to affinity, and is thus equal to the dissociation constant  $K_d$ . See, generally, Davies et al. (1990) Annual Rev. Biochem. 59:439-473.

25 An "antigen-binding site," or "binding portion" of an antibody refers to the part of the immunoglobulin molecule that participates in antigen binding. The antigen binding site is formed by amino acid residues of the N-terminal variable ("V") regions of the heavy ("H") and light ("L") chains. Three highly divergent stretches within the V regions of the heavy and light chains are referred to as "hypervariable  
30 regions" which are interposed between more conserved flanking stretches known as

"framework regions," or "FRs". Thus the term "FR" refers to amino acid sequences which are naturally found between and adjacent to hypervariable regions in immunoglobulins. In an antibody molecule, the three hypervariable regions of a light chain and the three hypervariable regions of a heavy chain are disposed relative to each other in three dimensional space to form an antigen-binding surface. The antigen-binding surface is complementary to the three-dimensional surface of a bound antigen, and the three hypervariable regions of each of the heavy and light chains are referred to as "complementarity-determining regions," or "CDRs."

Binding agents may be further capable of differentiating between patients with and without a cancer, such as prostate cancer, using the representative assays provided herein. For example, antibodies or other binding agents that bind to a tumor protein will preferably generate a signal indicating the presence of a cancer in at least about 20% of patients with the disease, more preferably at least about 30% of patients. Alternatively, or in addition, the antibody will generate a negative signal indicating the absence of the disease in at least about 90% of individuals without the cancer. To determine whether a binding agent satisfies this requirement, biological samples (*e.g.*, blood, sera, sputum, urine and/or tumor biopsies) from patients with and without a cancer (as determined using standard clinical tests) may be assayed as described herein for the presence of polypeptides that bind to the binding agent. Preferably, a statistically significant number of samples with and without the disease will be assayed. Each binding agent should satisfy the above criteria; however, those of ordinary skill in the art will recognize that binding agents may be used in combination to improve sensitivity.

Any agent that satisfies the above requirements may be a binding agent.

For example, a binding agent may be a ribosome, with or without a peptide component, an RNA molecule or a polypeptide. In a preferred embodiment, a binding agent is an antibody or an antigen-binding fragment thereof. Antibodies may be prepared by any of a variety of techniques known to those of ordinary skill in the art. *See, e.g.*, Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, antibodies can be produced by cell culture techniques, including the generation

of monoclonal antibodies as described herein, or via transfection of antibody genes into suitable bacterial or mammalian cell hosts, in order to allow for the production of recombinant antibodies. In one technique, an immunogen comprising the polypeptide is initially injected into any of a wide variety of mammals (*e.g.*, mice, rats, rabbits, sheep or goats). In this step, the polypeptides of this invention may serve as the immunogen without modification. Alternatively, particularly for relatively short polypeptides, a superior immune response may be elicited if the polypeptide is joined to a carrier protein, such as bovine serum albumin or keyhole limpet hemocyanin. The immunogen is injected into the animal host, preferably according to a predetermined schedule incorporating one or more booster immunizations, and the animals are bled periodically. Polyclonal antibodies specific for the polypeptide may then be purified from such antisera by, for example, affinity chromatography using the polypeptide coupled to a suitable solid support.

Monoclonal antibodies specific for an antigenic polypeptide of interest may be prepared, for example, using the technique of Kohler and Milstein, *Eur. J. Immunol.* 6:511-519, 1976, and improvements thereto. Briefly, these methods involve the preparation of immortal cell lines capable of producing antibodies having the desired specificity (*i.e.*, reactivity with the polypeptide of interest). Such cell lines may be produced, for example, from spleen cells obtained from an animal immunized as described above. The spleen cells are then immortalized by, for example, fusion with a myeloma cell fusion partner, preferably one that is syngeneic with the immunized animal. A variety of fusion techniques may be employed. For example, the spleen cells and myeloma cells may be combined with a nonionic detergent for a few minutes and then plated at low density on a selective medium that supports the growth of hybrid cells, but not myeloma cells. A preferred selection technique uses HAT (hypoxanthine, aminopterin, thymidine) selection. After a sufficient time, usually about 1 to 2 weeks, colonies of hybrids are observed. Single colonies are selected and their culture supernatants tested for binding activity against the polypeptide. Hybridomas having high reactivity and specificity are preferred.

Monoclonal antibodies may be isolated from the supernatants of growing hybridoma colonies. In addition, various techniques may be employed to enhance the yield, such as injection of the hybridoma cell line into the peritoneal cavity of a suitable vertebrate host, such as a mouse. Monoclonal antibodies may then be harvested from the ascites fluid or the blood. Contaminants may be removed from the antibodies by conventional techniques, such as chromatography, gel filtration, precipitation, and extraction. The polypeptides of this invention may be used in the purification process in, for example, an affinity chromatography step.

A number of therapeutically useful molecules are known in the art which comprise antigen-binding sites that are capable of exhibiting immunological binding properties of an antibody molecule. The proteolytic enzyme papain preferentially cleaves IgG molecules to yield several fragments, two of which (the "F(ab)" fragments) each comprise a covalent heterodimer that includes an intact antigen-binding site. The enzyme pepsin is able to cleave IgG molecules to provide several fragments, including the "F(ab)<sub>2</sub>" fragment which comprises both antigen-binding sites. An "Fv" fragment can be produced by preferential proteolytic cleavage of an IgM, and on rare occasions IgG or IgA immunoglobulin molecule. Fv fragments are, however, more commonly derived using recombinant techniques known in the art. The Fv fragment includes a non-covalent V<sub>H</sub>::V<sub>L</sub> heterodimer including an antigen-binding site which retains much of the antigen recognition and binding capabilities of the native antibody molecule. Inbar et al. (1972) Proc. Nat. Acad. Sci. USA 69:2659-2662; Hochman et al. (1976) Biochem 15:2706-2710; and Ehrlich et al. (1980) Biochem 19:4091-4096.

A single chain Fv ("sFv") polypeptide is a covalently linked V<sub>H</sub>::V<sub>L</sub> heterodimer which is expressed from a gene fusion including V<sub>H</sub>- and V<sub>L</sub>-encoding genes linked by a peptide-encoding linker. Huston et al. (1988) Proc. Nat. Acad. Sci. USA 85(16):5879-5883. A number of methods have been described to discern chemical structures for converting the naturally aggregated--but chemically separated--light and heavy polypeptide chains from an antibody V region into an sFv molecule which will fold into a three dimensional structure substantially similar to the structure of an

antigen-binding site. See, *e.g.*, U.S. Pat. Nos. 5,091,513 and 5,132,405, to Huston et al.; and U.S. Pat. No. 4,946,778, to Ladner et al.

Each of the above-described molecules includes a heavy chain and a light chain CDR set, respectively interposed between a heavy chain and a light chain FR set which provide support to the CDRs and define the spatial relationship of the CDRs relative to each other. As used herein, the term "CDR set" refers to the three hypervariable regions of a heavy or light chain V region. Proceeding from the N-terminus of a heavy or light chain, these regions are denoted as "CDR1," "CDR2," and "CDR3" respectively. An antigen-binding site, therefore, includes six CDRs, comprising the CDR set from each of a heavy and a light chain V region. A polypeptide comprising a single CDR, (*e.g.*, a CDR1, CDR2 or CDR3) is referred to herein as a "molecular recognition unit." Crystallographic analysis of a number of antigen-antibody complexes has demonstrated that the amino acid residues of CDRs form extensive contact with bound antigen, wherein the most extensive antigen contact is with the heavy chain CDR3. Thus, the molecular recognition units are primarily responsible for the specificity of an antigen-binding site.

As used herein, the term "FR set" refers to the four flanking amino acid sequences which frame the CDRs of a CDR set of a heavy or light chain V region. Some FR residues may contact bound antigen; however, FRs are primarily responsible for folding the V region into the antigen-binding site, particularly the FR residues directly adjacent to the CDRs. Within FRs, certain amino residues and certain structural features are very highly conserved. In this regard, all V region sequences contain an internal disulfide loop of around 90 amino acid residues. When the V regions fold into a binding-site, the CDRs are displayed as projecting loop motifs which form an antigen-binding surface. It is generally recognized that there are conserved structural regions of FRs which influence the folded shape of the CDR loops into certain "canonical" structures--regardless of the precise CDR amino acid sequence. Further, certain FR residues are known to participate in non-covalent interdomain contacts which stabilize the interaction of the antibody heavy and light chains.

A number of "humanized" antibody molecules comprising an antigen-binding site derived from a non-human immunoglobulin have been described, including chimeric antibodies having rodent V regions and their associated CDRs fused to human constant domains (Winter et al. (1991) *Nature* 349:293-299; Lobuglio et al. (1989) *Proc. Nat. Acad. Sci. USA* 86:4220-4224; Shaw et al. (1987) *J Immunol.* 138:4534-4538; and Brown et al. (1987) *Cancer Res.* 47:3577-3583), rodent CDRs grafted into a human supporting FR prior to fusion with an appropriate human antibody constant domain (Riechmann et al. (1988) *Nature* 332:323-327; Verhoeven et al. (1988) *Science* 239:1534-1536; and Jones et al. (1986) *Nature* 321:522-525), and rodent CDRs supported by recombinantly veneered rodent FRs (European Patent Publication No. 519,596, published Dec. 23, 1992). These "humanized" molecules are designed to minimize unwanted immunological response toward rodent antihuman antibody molecules which limits the duration and effectiveness of therapeutic applications of those moieties in human recipients.

As used herein, the terms "veneered FRs" and "recombinantly veneered FRs" refer to the selective replacement of FR residues from, *e.g.*, a rodent heavy or light chain V region, with human FR residues in order to provide a xenogeneic molecule comprising an antigen-binding site which retains substantially all of the native FR polypeptide folding structure. Veneering techniques are based on the understanding that the ligand binding characteristics of an antigen-binding site are determined primarily by the structure and relative disposition of the heavy and light chain CDR sets within the antigen-binding surface. Davies et al. (1990) *Ann. Rev. Biochem.* 59:439-473. Thus, antigen binding specificity can be preserved in a humanized antibody only wherein the CDR structures, their interaction with each other, and their interaction with the rest of the V region domains are carefully maintained. By using veneering techniques, exterior (*e.g.*, solvent-accessible) FR residues which are readily encountered by the immune system are selectively replaced with human residues to provide a hybrid molecule that comprises either a weakly immunogenic, or substantially non-immunogenic veneered surface.

The process of veneering makes use of the available sequence data for human antibody variable domains compiled by Kabat et al., in Sequences of Proteins of Immunological Interest, 4th ed., (U.S. Dept. of Health and Human Services, U.S. Government Printing Office, 1987), updates to the Kabat database, and other accessible U.S. and foreign databases (both nucleic acid and protein). Solvent accessibilities of V region amino acids can be deduced from the known three-dimensional structure for human and murine antibody fragments. There are two general steps in veneering a murine antigen-binding site. Initially, the FRs of the variable domains of an antibody molecule of interest are compared with corresponding FR sequences of human variable domains obtained from the above-identified sources. The most homologous human V regions are then compared residue by residue to corresponding murine amino acids. The residues in the murine FR which differ from the human counterpart are replaced by the residues present in the human moiety using recombinant techniques well known in the art. Residue switching is only carried out with moieties which are at least partially exposed (solvent accessible), and care is exercised in the replacement of amino acid residues which may have a significant effect on the tertiary structure of V region domains, such as proline, glycine and charged amino acids.

In this manner, the resultant "veneered" murine antigen-binding sites are thus designed to retain the murine CDR residues, the residues substantially adjacent to the CDRs, the residues identified as buried or mostly buried (solvent inaccessible), the residues believed to participate in non-covalent (e.g., electrostatic and hydrophobic) contacts between heavy and light chain domains, and the residues from conserved structural regions of the FRs which are believed to influence the "canonical" tertiary structures of the CDR loops. These design criteria are then used to prepare recombinant nucleotide sequences which combine the CDRs of both the heavy and light chain of a murine antigen-binding site into human-appearing FRs that can be used to transfect mammalian cells for the expression of recombinant human antibodies which exhibit the antigen specificity of the murine antibody molecule.

In another embodiment of the invention, monoclonal antibodies of the present invention may be coupled to one or more therapeutic agents. Suitable agents in

this regard include radionuclides, differentiation inducers, drugs, toxins, and derivatives thereof. Preferred radionuclides include  $^{90}\text{Y}$ ,  $^{123}\text{I}$ ,  $^{125}\text{I}$ ,  $^{131}\text{I}$ ,  $^{186}\text{Re}$ ,  $^{188}\text{Re}$ ,  $^{211}\text{At}$ , and  $^{212}\text{Bi}$ . Preferred drugs include methotrexate, and pyrimidine and purine analogs. Preferred differentiation inducers include phorbol esters and butyric acid. Preferred  
5 toxins include ricin, abrin, diptheria toxin, cholera toxin, gelonin, *Pseudomonas* exotoxin, *Shigella* toxin, and pokeweed antiviral protein.

A therapeutic agent may be coupled (*e.g.*, covalently bonded) to a suitable monoclonal antibody either directly or indirectly (*e.g.*, via a linker group). A direct reaction between an agent and an antibody is possible when each possesses a  
10 substituent capable of reacting with the other. For example, a nucleophilic group, such as an amino or sulfhydryl group, on one may be capable of reacting with a carbonyl-containing group, such as an anhydride or an acid halide, or with an alkyl group containing a good leaving group (*e.g.*, a halide) on the other.

Alternatively, it may be desirable to couple a therapeutic agent and an  
15 antibody via a linker group. A linker group can function as a spacer to distance an antibody from an agent in order to avoid interference with binding capabilities. A linker group can also serve to increase the chemical reactivity of a substituent on an agent or an antibody, and thus increase the coupling efficiency. An increase in chemical reactivity may also facilitate the use of agents, or functional groups on agents, which  
20 otherwise would not be possible.

It will be evident to those skilled in the art that a variety of bifunctional or polyfunctional reagents, both homo- and hetero-functional (such as those described in the catalog of the Pierce Chemical Co., Rockford, IL), may be employed as the linker group. Coupling may be effected, for example, through amino groups, carboxyl groups,  
25 sulfhydryl groups or oxidized carbohydrate residues. There are numerous references describing such methodology, *e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.

Where a therapeutic agent is more potent when free from the antibody portion of the immunoconjugates of the present invention, it may be desirable to use a linker group which is cleavable during or upon internalization into a cell. A number of  
30 different cleavable linker groups have been described. The mechanisms for the



intracellular release of an agent from these linker groups include cleavage by reduction of a disulfide bond (*e.g.*, U.S. Patent No. 4,489,710, to Spitler), by irradiation of a photolabile bond (*e.g.*, U.S. Patent No. 4,625,014, to Senter et al.), by hydrolysis of derivatized amino acid side chains (*e.g.*, U.S. Patent No. 4,638,045, to Kohn et al.), by  
5 serum complement-mediated hydrolysis (*e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.), and acid-catalyzed hydrolysis (*e.g.*, U.S. Patent No. 4,569,789, to Blattler et al.).

It may be desirable to couple more than one agent to an antibody. In one embodiment, multiple molecules of an agent are coupled to one antibody molecule. In another embodiment, more than one type of agent may be coupled to one antibody.  
10 Regardless of the particular embodiment, immunoconjugates with more than one agent may be prepared in a variety of ways. For example, more than one agent may be coupled directly to an antibody molecule, or linkers that provide multiple sites for attachment can be used. Alternatively, a carrier can be used.

A carrier may bear the agents in a variety of ways, including covalent  
15 bonding either directly or via a linker group. Suitable carriers include proteins such as albumins (*e.g.*, U.S. Patent No. 4,507,234, to Kato et al.), peptides and polysaccharides such as aminodextran (*e.g.*, U.S. Patent No. 4,699,784, to Shih et al.). A carrier may also bear an agent by noncovalent bonding or by encapsulation, such as within a liposome vesicle (*e.g.*, U.S. Patent Nos. 4,429,008 and 4,873,088). Carriers specific for  
20 radionuclide agents include radiohalogenated small molecules and chelating compounds. For example, U.S. Patent No. 4,735,792 discloses representative radiohalogenated small molecules and their synthesis. A radionuclide chelate may be formed from chelating compounds that include those containing nitrogen and sulfur atoms as the donor atoms for binding the metal, or metal oxide, radionuclide. For  
25 example, U.S. Patent No. 4,673,562, to Davison et al. discloses representative chelating compounds and their synthesis.

### T Cell Compositions

The present invention, in another aspect, provides T cells specific for a tumor polypeptide disclosed herein, or for a variant or derivative thereof. Such cells

may generally be prepared *in vitro* or *ex vivo*, using standard procedures. For example, T cells may be isolated from bone marrow, peripheral blood, or a fraction of bone marrow or peripheral blood of a patient, using a commercially available cell separation system, such as the Isolex™ System, available from Nexell Therapeutics, Inc. (Irvine, CA; see also U.S. Patent No. 5,240,856; U.S. Patent No. 5,215,926; WO 89/06280; WO 91/16116 and WO 92/07243). Alternatively, T cells may be derived from related or unrelated humans, non-human mammals, cell lines or cultures.

T cells may be stimulated with a polypeptide, polynucleotide encoding a polypeptide and/or an antigen presenting cell (APC) that expresses such a polypeptide. Such stimulation is performed under conditions and for a time sufficient to permit the generation of T cells that are specific for the polypeptide of interest. Preferably, a tumor polypeptide or polynucleotide of the invention is present within a delivery vehicle, such as a microsphere, to facilitate the generation of specific T cells.

T cells are considered to be specific for a polypeptide of the present invention if the T cells specifically proliferate, secrete cytokines or kill target cells coated with the polypeptide or expressing a gene encoding the polypeptide. T cell specificity may be evaluated using any of a variety of standard techniques. For example, within a chromium release assay or proliferation assay, a stimulation index of more than two fold increase in lysis and/or proliferation, compared to negative controls, indicates T cell specificity. Such assays may be performed, for example, as described in Chen et al., *Cancer Res.* 54:1065-1070, 1994. Alternatively, detection of the proliferation of T cells may be accomplished by a variety of known techniques. For example, T cell proliferation can be detected by measuring an increased rate of DNA synthesis (*e.g.*, by pulse-labeling cultures of T cells with tritiated thymidine and measuring the amount of tritiated thymidine incorporated into DNA). Contact with a tumor polypeptide (100 ng/ml - 100 µg/ml, preferably 200 ng/ml - 25 µg/ml) for 3 - 7 days will typically result in at least a two fold increase in proliferation of the T cells. Contact as described above for 2-3 hours should result in activation of the T cells, as measured using standard cytokine assays in which a two fold increase in the level of cytokine release (*e.g.*, TNF or IFN-γ) is indicative of T cell activation (*see* Coligan et

al., Current Protocols in Immunology, vol. 1, Wiley Interscience (Greene 1998)). T cells that have been activated in response to a tumor polypeptide, polynucleotide or polypeptide-expressing APC may be CD4<sup>+</sup> and/or CD8<sup>+</sup>. Tumor polypeptide-specific T cells may be expanded using standard techniques. Within preferred embodiments, the T cells are derived from a patient, a related donor or an unrelated donor, and are administered to the patient following stimulation and expansion.

For therapeutic purposes, CD4<sup>+</sup> or CD8<sup>+</sup> T cells that proliferate in response to a tumor polypeptide, polynucleotide or APC can be expanded in number either *in vitro* or *in vivo*. Proliferation of such T cells *in vitro* may be accomplished in a variety of ways. For example, the T cells can be re-exposed to a tumor polypeptide, or a short peptide corresponding to an immunogenic portion of such a polypeptide, with or without the addition of T cell growth factors, such as interleukin-2, and/or stimulator cells that synthesize a tumor polypeptide. Alternatively, one or more T cells that proliferate in the presence of the tumor polypeptide can be expanded in number by cloning. Methods for cloning cells are well known in the art, and include limiting dilution.

#### Pharmaceutical Compositions

In additional embodiments, the present invention concerns formulation of one or more of the polynucleotide, polypeptide, T-cell and/or antibody compositions disclosed herein in pharmaceutically-acceptable carriers for administration to a cell or an animal, either alone, or in combination with one or more other modalities of therapy.

It will be understood that, if desired, a composition as disclosed herein may be administered in combination with other agents as well, such as, *e.g.*, other proteins or polypeptides or various pharmaceutically-active agents. In fact, there is virtually no limit to other components that may also be included, given that the additional agents do not cause a significant adverse effect upon contact with the target cells or host tissues. The compositions may thus be delivered along with various other agents as required in the particular instance. Such compositions may be purified from host cells or other biological sources, or alternatively may be chemically synthesized as

described herein. Likewise, such compositions may further comprise substituted or derivatized RNA or DNA compositions.

Therefore, in another aspect of the present invention, pharmaceutical compositions are provided comprising one or more of the polynucleotide, polypeptide, antibody, and/or T-cell compositions described herein in combination with a physiologically acceptable carrier. In certain preferred embodiments, the pharmaceutical compositions of the invention comprise immunogenic polynucleotide and/or polypeptide compositions of the invention for use in prophylactic and therapeutic vaccine applications. Vaccine preparation is generally described in, for example, M.F. Powell and M.J. Newman, eds., "Vaccine Design (the subunit and adjuvant approach)," Plenum Press (NY, 1995). Generally, such compositions will comprise one or more polynucleotide and/or polypeptide compositions of the present invention in combination with one or more immunostimulants.

It will be apparent that any of the pharmaceutical compositions described herein can contain pharmaceutically acceptable salts of the polynucleotides and polypeptides of the invention. Such salts can be prepared, for example, from pharmaceutically acceptable non-toxic bases, including organic bases (e.g., salts of primary, secondary and tertiary amines and basic amino acids) and inorganic bases (e.g., sodium, potassium, lithium, ammonium, calcium and magnesium salts).

In another embodiment, illustrative immunogenic compositions, e.g., vaccine compositions, of the present invention comprise DNA encoding one or more of the polypeptides as described above, such that the polypeptide is generated *in situ*. As noted above, the polynucleotide may be administered within any of a variety of delivery systems known to those of ordinary skill in the art. Indeed, numerous gene delivery techniques are well known in the art, such as those described by Rolland, *Crit. Rev. Therap. Drug Carrier Systems* 15:143-198, 1998, and references cited therein. Appropriate polynucleotide expression systems will, of course, contain the necessary regulatory DNA regulatory sequences for expression in a patient (such as a suitable promoter and terminating signal). Alternatively, bacterial delivery systems may involve

the administration of a bacterium (such as *Bacillus-Calmette-Guerrin*) that expresses an immunogenic portion of the polypeptide on its cell surface or secretes such an epitope.

Therefore, in certain embodiments, polynucleotides encoding immunogenic polypeptides described herein are introduced into suitable mammalian host cells for expression using any of a number of known viral-based systems. In one illustrative embodiment, retroviruses provide a convenient and effective platform for gene delivery systems. A selected nucleotide sequence encoding a polypeptide of the present invention can be inserted into a vector and packaged in retroviral particles using techniques known in the art. The recombinant virus can then be isolated and delivered to a subject. A number of illustrative retroviral systems have been described (*e.g.*, U.S. Pat. No. 5,219,740; Miller and Rosman (1989) *BioTechniques* 7:980-990; Miller, A. D. (1990) *Human Gene Therapy* 1:5-14; Scarpa et al. (1991) *Virology* 180:849-852; Burns et al. (1993) *Proc. Natl. Acad. Sci. USA* 90:8033-8037; and Boris-Lawrie and Temin (1993) *Cur. Opin. Genet. Develop.* 3:102-109.

In addition, a number of illustrative adenovirus-based systems have also been described. Unlike retroviruses which integrate into the host genome, adenoviruses persist extrachromosomally thus minimizing the risks associated with insertional mutagenesis (Haj-Ahmad and Graham (1986) *J. Virol.* 57:267-274; Bett et al. (1993) *J. Virol.* 67:5911-5921; Mittereder et al. (1994) *Human Gene Therapy* 5:717-729; Seth et al. (1994) *J. Virol.* 68:933-940; Barr et al. (1994) *Gene Therapy* 1:51-58; Berkner, K. L. (1988) *BioTechniques* 6:616-629; and Rich et al. (1993) *Human Gene Therapy* 4:461-476).

Various adeno-associated virus (AAV) vector systems have also been developed for polynucleotide delivery. AAV vectors can be readily constructed using techniques well known in the art. See, *e.g.*, U.S. Pat. Nos. 5,173,414 and 5,139,941; International Publication Nos. WO 92/01070 and WO 93/03769; Lebkowski et al. (1988) *Molec. Cell. Biol.* 8:3988-3996; Vincent et al. (1990) *Vaccines* 90 (Cold Spring Harbor Laboratory Press); Carter, B. J. (1992) *Current Opinion in Biotechnology* 3:533-539; Muzyczka, N. (1992) *Current Topics in Microbiol. and Immunol.* 158:97-129;

Kotin, R. M. (1994) *Human Gene Therapy* 5:793-801; Shelling and Smith (1994) *Gene Therapy* 1:165-169; and Zhou et al. (1994) *J. Exp. Med.* 179:1867-1875.

Additional viral vectors useful for delivering the polynucleotides encoding polypeptides of the present invention by gene transfer include those derived from the pox family of viruses, such as vaccinia virus and avian poxvirus. By way of example, vaccinia virus recombinants expressing the novel molecules can be constructed as follows. The DNA encoding a polypeptide is first inserted into an appropriate vector so that it is adjacent to a vaccinia promoter and flanking vaccinia DNA sequences, such as the sequence encoding thymidine kinase (TK). This vector is then used to transfect cells which are simultaneously infected with vaccinia. Homologous recombination serves to insert the vaccinia promoter plus the gene encoding the polypeptide of interest into the viral genome. The resulting TK.sup.(-) recombinant can be selected by culturing the cells in the presence of 5-bromodeoxyuridine and picking viral plaques resistant thereto.

A vaccinia-based infection/transfection system can be conveniently used to provide for inducible, transient expression or coexpression of one or more polypeptides described herein in host cells of an organism. In this particular system, cells are first infected in vitro with a vaccinia virus recombinant that encodes the bacteriophage T7 RNA polymerase. This polymerase displays exquisite specificity in that it only transcribes templates bearing T7 promoters. Following infection, cells are transfected with the polynucleotide or polynucleotides of interest, driven by a T7 promoter. The polymerase expressed in the cytoplasm from the vaccinia virus recombinant transcribes the transfected DNA into RNA which is then translated into polypeptide by the host translational machinery. The method provides for high level, transient, cytoplasmic production of large quantities of RNA and its translation products. See, e.g., Elroy-Stein and Moss, *Proc. Natl. Acad. Sci. USA* (1990) 87:6743-6747; Fuerst et al. *Proc. Natl. Acad. Sci. USA* (1986) 83:8122-8126.

Alternatively, avipoxviruses, such as the fowlpox and canarypox viruses, can also be used to deliver the coding sequences of interest. Recombinant avipox viruses, expressing immunogens from mammalian pathogens, are known to confer

protective immunity when administered to non-avian species. The use of an Avipox vector is particularly desirable in human and other mammalian species since members of the Avipox genus can only productively replicate in susceptible avian species and therefore are not infective in mammalian cells. Methods for producing recombinant  
5 Avipoxviruses are known in the art and employ genetic recombination, as described above with respect to the production of vaccinia viruses. See, *e.g.*, WO 91/12882; WO 89/03429; and WO 92/03545.

Any of a number of alphavirus vectors can also be used for delivery of polynucleotide compositions of the present invention, such as those vectors described in  
10 U.S. Patent Nos. 5,843,723; 6,015,686; 6,008,035 and 6,015,694. Certain vectors based on Venezuelan Equine Encephalitis (VEE) can also be used, illustrative examples of which can be found in U.S. Patent Nos. 5,505,947 and 5,643,576.

Moreover, molecular conjugate vectors, such as the adenovirus chimeric vectors described in Michael et al. *J. Biol. Chem.* (1993) 268:6866-6869 and Wagner et  
15 al. *Proc. Natl. Acad. Sci. USA* (1992) 89:6099-6103, can also be used for gene delivery under the invention.

Additional illustrative information on these and other known viral-based delivery systems can be found, for example, in Fisher-Hoch et al., *Proc. Natl. Acad. Sci. USA* 86:317-321, 1989; Flexner et al., *Ann. N.Y. Acad. Sci.* 569:86-103, 1989; Flexner et al., *Vaccine* 8:17-21, 1990; U.S. Patent Nos. 4,603,112, 4,769,330, and 5,017,487;  
20 WO 89/01973; U.S. Patent No. 4,777,127; GB 2,200,651; EP 0,345,242; WO 91/02805; Berkner, *Biotechniques* 6:616-627, 1988; Rosenfeld et al., *Science* 252:431-434, 1991; Kolls et al., *Proc. Natl. Acad. Sci. USA* 91:215-219, 1994; Kass-Eisler et al., *Proc. Natl. Acad. Sci. USA* 90:11498-11502, 1993; Guzman et al.,  
25 *Circulation* 88:2838-2848, 1993; and Guzman et al., *Cir. Res.* 73:1202-1207, 1993.

In certain embodiments, a polynucleotide may be integrated into the genome of a target cell. This integration may be in a specific location and orientation *via* homologous recombination (gene replacement) or it may be integrated in a random, non-specific location (gene augmentation). In yet further embodiments, the  
30 polynucleotide may be stably maintained in the cell as a separate, episomal segment of

DNA. Such polynucleotide segments or "episomes" encode sequences sufficient to permit maintenance and replication independent of or in synchronization with the host cell cycle. The manner in which the expression construct is delivered to a cell and where in the cell the polynucleotide remains is dependent on the type of expression  
5 construct employed.

In another embodiment of the invention, a polynucleotide is administered/delivered as "naked" DNA, for example as described in Ulmer et al., *Science* 259:1745-1749, 1993 and reviewed by Cohen, *Science* 259:1691-1692, 1993. The uptake of naked DNA may be increased by coating the DNA onto biodegradable  
10 beads, which are efficiently transported into the cells.

In still another embodiment, a composition of the present invention can be delivered via a particle bombardment approach, many of which have been described. In one illustrative example, gas-driven particle acceleration can be achieved with devices such as those manufactured by Powderject Pharmaceuticals PLC (Oxford, UK)  
15 and Powderject Vaccines Inc. (Madison, WI), some examples of which are described in U.S. Patent Nos. 5,846,796; 6,010,478; 5,865,796; 5,584,807; and EP Patent No. 0500 799. This approach offers a needle-free delivery approach wherein a dry powder formulation of microscopic particles, such as polynucleotide or polypeptide particles, are accelerated to high speed within a helium gas jet generated by a hand held device,  
20 propelling the particles into a target tissue of interest.

In a related embodiment, other devices and methods that may be useful for gas-driven needle-less injection of compositions of the present invention include those provided by Bioject, Inc. (Portland, OR), some examples of which are described in U.S. Patent Nos. 4,790,824; 5,064,413; 5,312,335; 5,383,851; 5,399,163; 5,520,639  
25 and 5,993,412.

According to another embodiment, the pharmaceutical compositions described herein will comprise one or more immunostimulants in addition to the immunogenic polynucleotide, polypeptide, antibody, T-cell and/or APC compositions of this invention. An immunostimulant refers to essentially any substance that enhances  
30 or potentiates an immune response (antibody and/or cell-mediated) to an exogenous



antigen. One preferred type of immunostimulant comprises an adjuvant. Many adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a stimulator of immune responses, such as lipid A, *Bordetella pertussis* or *Mycobacterium tuberculosis* derived proteins.

5 Certain adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories, Detroit, MI); Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ); AS-2 (SmithKline Beecham, Philadelphia, PA); aluminum salts such as aluminum hydroxide gel (alum) or aluminum phosphate; salts of calcium, iron or zinc; an insoluble suspension of acylated tyrosine; acylated

10 sugars; cationically or anionically derivatized polysaccharides; polyphosphazenes; biodegradable microspheres; monophosphoryl lipid A and quil A. Cytokines, such as GM-CSF, interleukin-2, -7, -12, and other like growth factors, may also be used as adjuvants.

Within certain embodiments of the invention, the adjuvant composition

15 is preferably one that induces an immune response predominantly of the Th1 type. High levels of Th1-type cytokines (e.g., IFN- $\gamma$ , TNF $\alpha$ , IL-2 and IL-12) tend to favor the induction of cell mediated immune responses to an administered antigen. In contrast, high levels of Th2-type cytokines (e.g., IL-4, IL-5, IL-6 and IL-10) tend to favor the induction of humoral immune responses. Following application of a vaccine as

20 provided herein, a patient will support an immune response that includes Th1- and Th2-type responses. Within a preferred embodiment, in which a response is predominantly Th1-type, the level of Th1-type cytokines will increase to a greater extent than the level of Th2-type cytokines. The levels of these cytokines may be readily assessed using standard assays. For a review of the families of cytokines, see Mosmann and Coffman,

25 *Ann. Rev. Immunol.* 7:145-173, 1989.

Certain preferred adjuvants for eliciting a predominantly Th1-type response include, for example, a combination of monophosphoryl lipid A, preferably 3-de-O-acylated monophosphoryl lipid A, together with an aluminum salt. MPL<sup>®</sup> adjuvants are available from Corixa Corporation (Seattle, WA; see, for example, US

30 Patent Nos. 4,436,727; 4,877,611; 4,866,034 and 4,912,094). CpG-containing

oligonucleotides (in which the CpG dinucleotide is unmethylated) also induce a predominantly Th1 response. Such oligonucleotides are well known and are described, for example, in WO 96/02555, WO 99/33488 and U.S. Patent Nos. 6,008,200 and 5,856,462. Immunostimulatory DNA sequences are also described, for example, by  
5 Sato et al., *Science* 273:352, 1996. Another preferred adjuvant comprises a saponin, such as Quil A, or derivatives thereof, including QS21 and QS7 (Aquila Biopharmaceuticals Inc., Framingham, MA); Escin; Digitonin; or *Gypsophila* or *Chenopodium quinoa* saponins. Other preferred formulations include more than one saponin in the adjuvant combinations of the present invention, for example  
10 combinations of at least two of the following group comprising QS21, QS7, Quil A,  $\beta$ -escin, or digitonin.

Alternatively the saponin formulations may be combined with vaccine vehicles composed of chitosan or other polycationic polymers, polylactide and polylactide-co-glycolide particles, poly-N-acetyl glucosamine-based polymer matrix,  
15 particles composed of polysaccharides or chemically modified polysaccharides, liposomes and lipid-based particles, particles composed of glycerol monoesters, etc. The saponins may also be formulated in the presence of cholesterol to form particulate structures such as liposomes or ISCOMs. Furthermore, the saponins may be formulated together with a polyoxyethylene ether or ester, in either a non-particulate solution or  
20 suspension, or in a particulate structure such as a paucilamellar liposome or ISCOM. The saponins may also be formulated with excipients such as Carbopol<sup>R</sup> to increase viscosity, or may be formulated in a dry powder form with a powder excipient such as lactose.

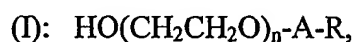
In one preferred embodiment, the adjuvant system includes the  
25 combination of a monophosphoryl lipid A and a saponin derivative, such as the combination of QS21 and 3D-MPL<sup>®</sup> adjuvant, as described in WO 94/00153, or a less reactogenic composition where the QS21 is quenched with cholesterol, as described in WO 96/33739. Other preferred formulations comprise an oil-in-water emulsion and tocopherol. Another particularly preferred adjuvant formulation employing QS21, 3D-

MPL<sup>®</sup> adjuvant and tocopherol in an oil-in-water emulsion is described in WO 95/17210.

Another enhanced adjuvant system involves the combination of a CpG-containing oligonucleotide and a saponin derivative particularly the combination of CpG and QS21 is disclosed in WO 00/09159. Preferably the formulation additionally comprises an oil in water emulsion and tocopherol.

Additional illustrative adjuvants for use in the pharmaceutical compositions of the invention include Montanide ISA 720 (Seppic, France), SAF (Chiron, California, United States), ISCOMS (CSL), MF-59 (Chiron), the SBAS series of adjuvants (*e.g.*, SBAS-2 or SBAS-4, available from SmithKline Beecham, Rixensart, Belgium), Detox (Enhanzyn<sup>®</sup>; Corixa, Hamilton, MT), RC-529 (Corixa, Hamilton, MT) and other aminoalkyl glucosaminide 4-phosphates (AGPs), such as those described in pending U.S. Patent Application Serial Nos. 08/853,826 and 09/074,720, the disclosures of which are incorporated herein by reference in their entireties, and polyoxyethylene ether adjuvants such as those described in WO 99/52549A1.

Other preferred adjuvants include adjuvant molecules of the general formula



wherein,  $n$  is 1-50,  $A$  is a bond or  $-\text{C}(\text{O})-$ ,  $R$  is  $\text{C}_{1-50}$  alkyl or Phenyl  $\text{C}_{1-50}$  alkyl.

One embodiment of the present invention consists of a vaccine formulation comprising a polyoxyethylene ether of general formula (I), wherein  $n$  is between 1 and 50, preferably 4-24, most preferably 9; the  $R$  component is  $\text{C}_{1-50}$ , preferably  $\text{C}_4\text{-C}_{20}$  alkyl and most preferably  $\text{C}_{12}$  alkyl, and  $A$  is a bond. The concentration of the polyoxyethylene ethers should be in the range 0.1-20%, preferably from 0.1-10%, and most preferably in the range 0.1-1%. Preferred polyoxyethylene ethers are selected from the following group: polyoxyethylene-9-lauryl ether, polyoxyethylene-9-stearyl ether, polyoxyethylene-8-stearyl ether, polyoxyethylene-4-lauryl ether, polyoxyethylene-35-lauryl ether, and polyoxyethylene-23-lauryl ether. Polyoxyethylene ethers such as polyoxyethylene lauryl ether are described in the Merck index (12<sup>th</sup> edition: entry 7717). These adjuvant molecules are described in WO

99/52549. The polyoxyethylene ether according to the general formula (I) above may, if desired, be combined with another adjuvant. For example, a preferred adjuvant combination is preferably with CpG as described in the pending UK patent application GB 9820956.2.

5                   According to another embodiment of this invention, an immunogenic composition described herein is delivered to a host via antigen presenting cells (APCs), such as dendritic cells, macrophages, B cells, monocytes and other cells that may be engineered to be efficient APCs. Such cells may, but need not, be genetically modified to increase the capacity for presenting the antigen, to improve activation and/or  
10 maintenance of the T cell response, to have anti-tumor effects *per se* and/or to be immunologically compatible with the receiver (*i.e.*, matched HLA haplotype). APCs may generally be isolated from any of a variety of biological fluids and organs, including tumor and peritumoral tissues, and may be autologous, allogeneic, syngeneic or xenogeneic cells.

15                   Certain preferred embodiments of the present invention use dendritic cells or progenitors thereof as antigen-presenting cells. Dendritic cells are highly potent APCs (Banchereau and Steinman, *Nature* 392:245-251, 1998) and have been shown to be effective as a physiological adjuvant for eliciting prophylactic or therapeutic antitumor immunity (*see* Timmerman and Levy, *Ann. Rev. Med.* 50:507-529, 1999). In  
20 general, dendritic cells may be identified based on their typical shape (stellate *in situ*, with marked cytoplasmic processes (dendrites) visible *in vitro*), their ability to take up, process and present antigens with high efficiency and their ability to activate naïve T cell responses. Dendritic cells may, of course, be engineered to express specific cell-surface receptors or ligands that are not commonly found on dendritic cells *in vivo* or *ex*  
25 *vivo*, and such modified dendritic cells are contemplated by the present invention. As an alternative to dendritic cells, secreted vesicles antigen-loaded dendritic cells (called exosomes) may be used within a vaccine (*see* Zitvogel et al., *Nature Med.* 4:594-600, 1998).

                  Dendritic cells and progenitors may be obtained from peripheral blood,  
30 bone marrow, tumor-infiltrating cells, peritumoral tissues-infiltrating cells, lymph

nodes, spleen, skin, umbilical cord blood or any other suitable tissue or fluid. For example, dendritic cells may be differentiated *ex vivo* by adding a combination of cytokines such as GM-CSF, IL-4, IL-13 and/or TNF $\alpha$  to cultures of monocytes harvested from peripheral blood. Alternatively, CD34 positive cells harvested from peripheral blood, umbilical cord blood or bone marrow may be differentiated into dendritic cells by adding to the culture medium combinations of GM-CSF, IL-3, TNF $\alpha$ , CD40 ligand, LPS, flt3 ligand and/or other compound(s) that induce differentiation, maturation and proliferation of dendritic cells.

Dendritic cells are conveniently categorized as "immature" and "mature" cells, which allows a simple way to discriminate between two well characterized phenotypes. However, this nomenclature should not be construed to exclude all possible intermediate stages of differentiation. Immature dendritic cells are characterized as APC with a high capacity for antigen uptake and processing, which correlates with the high expression of Fc $\gamma$  receptor and mannose receptor. The mature phenotype is typically characterized by a lower expression of these markers, but a high expression of cell surface molecules responsible for T cell activation such as class I and class II MHC, adhesion molecules (*e.g.*, CD54 and CD11) and costimulatory molecules (*e.g.*, CD40, CD80, CD86 and 4-1BB).

APCs may generally be transfected with a polynucleotide of the invention (or portion or other variant thereof) such that the encoded polypeptide, or an immunogenic portion thereof, is expressed on the cell surface. Such transfection may take place *ex vivo*, and a pharmaceutical composition comprising such transfected cells may then be used for therapeutic purposes, as described herein. Alternatively, a gene delivery vehicle that targets a dendritic or other antigen presenting cell may be administered to a patient, resulting in transfection that occurs *in vivo*. *In vivo* and *ex vivo* transfection of dendritic cells, for example, may generally be performed using any methods known in the art, such as those described in WO 97/24447, or the gene gun approach described by Mahvi et al., *Immunology and cell Biology* 75:456-460, 1997. Antigen loading of dendritic cells may be achieved by incubating dendritic cells or progenitor cells with the tumor polypeptide, DNA (naked or within a plasmid vector) or

RNA; or with antigen-expressing recombinant bacterium or viruses (*e.g.*, vaccinia, fowlpox, adenovirus or lentivirus vectors). Prior to loading, the polypeptide may be covalently conjugated to an immunological partner that provides T cell help (*e.g.*, a carrier molecule). Alternatively, a dendritic cell may be pulsed with a non-conjugated immunological partner, separately or in the presence of the polypeptide.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will typically vary depending on the mode of administration. Compositions of the present invention may be formulated for any appropriate manner of administration, including for example, topical, oral, nasal, mucosal, intravenous, intracranial, intraperitoneal, subcutaneous and intramuscular administration.

Carriers for use within such pharmaceutical compositions are biocompatible, and may also be biodegradable. In certain embodiments, the formulation preferably provides a relatively constant level of active component release. In other embodiments, however, a more rapid rate of release immediately upon administration may be desired. The formulation of such compositions is well within the level of ordinary skill in the art using known techniques. Illustrative carriers useful in this regard include microparticles of poly(lactide-co-glycolide), polyacrylate, latex, starch, cellulose, dextran and the like. Other illustrative delayed-release carriers include supramolecular biovectors, which comprise a non-liquid hydrophilic core (*e.g.*, a cross-linked polysaccharide or oligosaccharide) and, optionally, an external layer comprising an amphiphilic compound, such as a phospholipid (*see e.g.*, U.S. Patent No. 5,151,254 and PCT applications WO 94/20078, WO/94/23701 and WO 96/06638). The amount of active compound contained within a sustained release formulation depends upon the site of implantation, the rate and expected duration of release and the nature of the condition to be treated or prevented.

In another illustrative embodiment, biodegradable microspheres (*e.g.*, polylactate polyglycolate) are employed as carriers for the compositions of this invention. Suitable biodegradable microspheres are disclosed, for example, in U.S. Patent Nos. 4,897,268; 5,075,109; 5,928,647; 5,811,128; 5,820,883; 5,853,763;

5,814,344, 5,407,609 and 5,942,252. Modified hepatitis B core protein carrier systems, such as described in WO/99 40934, and references cited therein, will also be useful for many applications. Another illustrative carrier/delivery system employs a carrier comprising particulate-protein complexes, such as those described in U.S. Patent No. 5,928,647, which are capable of inducing a class I-restricted cytotoxic T lymphocyte responses in a host.

The pharmaceutical compositions of the invention will often further comprise one or more buffers (*e.g.*, neutral buffered saline or phosphate buffered saline), carbohydrates (*e.g.*, glucose, mannose, sucrose or dextrans), mannitol, proteins, polypeptides or amino acids such as glycine, antioxidants, bacteriostats, chelating agents such as EDTA or glutathione, adjuvants (*e.g.*, aluminum hydroxide), solutes that render the formulation isotonic, hypotonic or weakly hypertonic with the blood of a recipient, suspending agents, thickening agents and/or preservatives. Alternatively, compositions of the present invention may be formulated as a lyophilizate.

The pharmaceutical compositions described herein may be presented in unit-dose or multi-dose containers, such as sealed ampoules or vials. Such containers are typically sealed in such a way to preserve the sterility and stability of the formulation until use. In general, formulations may be stored as suspensions, solutions or emulsions in oily or aqueous vehicles. Alternatively, a pharmaceutical composition may be stored in a freeze-dried condition requiring only the addition of a sterile liquid carrier immediately prior to use.

The development of suitable dosing and treatment regimens for using the particular compositions described herein in a variety of treatment regimens, including *e.g.*, oral, parenteral, intravenous, intranasal, and intramuscular administration and formulation, is well known in the art, some of which are briefly discussed below for general purposes of illustration.

In certain applications, the pharmaceutical compositions disclosed herein may be delivered *via* oral administration to an animal. As such, these compositions may be formulated with an inert diluent or with an assimilable edible carrier, or they

may be enclosed in hard- or soft-shell gelatin capsule, or they may be compressed into tablets, or they may be incorporated directly with the food of the diet.

The active compounds may even be incorporated with excipients and used in the form of ingestible tablets, buccal tables, troches, capsules, elixirs, suspensions, syrups, wafers, and the like (see, for example, Mathiowitz *et al.*, Nature 1997 Mar 27;386(6623):410-4; Hwang *et al.*, Crit Rev Ther Drug Carrier Syst 1998;15(3):243-84; U. S. Patent 5,641,515; U. S. Patent 5,580,579 and U. S. Patent 5,792,451). Tablets, troches, pills, capsules and the like may also contain any of a variety of additional components, for example, a binder, such as gum tragacanth, acacia, cornstarch, or gelatin; excipients, such as dicalcium phosphate; a disintegrating agent, such as corn starch, potato starch, alginic acid and the like; a lubricant, such as magnesium stearate; and a sweetening agent, such as sucrose, lactose or saccharin may be added or a flavoring agent, such as peppermint, oil of wintergreen, or cherry flavoring. When the dosage unit form is a capsule, it may contain, in addition to materials of the above type, a liquid carrier. Various other materials may be present as coatings or to otherwise modify the physical form of the dosage unit. For instance, tablets, pills, or capsules may be coated with shellac, sugar, or both. Of course, any material used in preparing any dosage unit form should be pharmaceutically pure and substantially non-toxic in the amounts employed. In addition, the active compounds may be incorporated into sustained-release preparation and formulations.

Typically, these formulations will contain at least about 0.1% of the active compound or more, although the percentage of the active ingredient(s) may, of course, be varied and may conveniently be between about 1 or 2% and about 60% or 70% or more of the weight or volume of the total formulation. Naturally, the amount of active compound(s) in each therapeutically useful composition may be prepared in such a way that a suitable dosage will be obtained in any given unit dose of the compound. Factors such as solubility, bioavailability, biological half-life, route of administration, product shelf life, as well as other pharmacological considerations will be contemplated by one skilled in the art of preparing such pharmaceutical formulations, and as such, a variety of dosages and treatment regimens may be desirable.



For oral administration, the compositions of the present invention may alternatively be incorporated with one or more excipients in the form of a mouthwash, dentifrice, buccal tablet, oral spray, or sublingual orally-administered formulation. Alternatively, the active ingredient may be incorporated into an oral solution such as one containing sodium borate, glycerin and potassium bicarbonate, or dispersed in a dentifrice, or added in a therapeutically-effective amount to a composition that may include water, binders, abrasives, flavoring agents, foaming agents, and humectants. Alternatively the compositions may be fashioned into a tablet or solution form that may be placed under the tongue or otherwise dissolved in the mouth.

In certain circumstances it will be desirable to deliver the pharmaceutical compositions disclosed herein parenterally, intravenously, intramuscularly, or even intraperitoneally. Such approaches are well known to the skilled artisan, some of which are further described, for example, in U. S. Patent 5,543,158; U. S. Patent 5,641,515 and U. S. Patent 5,399,363. In certain embodiments, solutions of the active compounds as free base or pharmacologically acceptable salts may be prepared in water suitably mixed with a surfactant, such as hydroxypropylcellulose. Dispersions may also be prepared in glycerol, liquid polyethylene glycols, and mixtures thereof and in oils. Under ordinary conditions of storage and use, these preparations generally will contain a preservative to prevent the growth of microorganisms.

Illustrative pharmaceutical forms suitable for injectable use include sterile aqueous solutions or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersions (for example, see U. S. Patent 5,466,468). In all cases the form must be sterile and must be fluid to the extent that easy syringability exists. It must be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms, such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (e.g., glycerol, propylene glycol, and liquid polyethylene glycol, and the like), suitable mixtures thereof, and/or vegetable oils. Proper fluidity may be maintained, for example, by the use of a coating, such as lecithin, by the maintenance of the required particle size in the case of dispersion and/or

by the use of surfactants. The prevention of the action of microorganisms can be facilitated by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, sorbic acid, thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars or sodium chloride.

- 5 Prolonged absorption of the injectable compositions can be brought about by the use in the compositions of agents delaying absorption, for example, aluminum monostearate and gelatin.

In one embodiment, for parenteral administration in an aqueous solution, the solution should be suitably buffered if necessary and the liquid diluent first rendered  
10 isotonic with sufficient saline or glucose. These particular aqueous solutions are especially suitable for intravenous, intramuscular, subcutaneous and intraperitoneal administration. In this connection, a sterile aqueous medium that can be employed will be known to those of skill in the art in light of the present disclosure. For example, one dosage may be dissolved in 1 ml of isotonic NaCl solution and either added to 1000 ml  
15 of hypodermoclysis fluid or injected at the proposed site of infusion, (see for example, "Remington's Pharmaceutical Sciences" 15th Edition, pages 1035-1038 and 1570-1580). Some variation in dosage will necessarily occur depending on the condition of the subject being treated. Moreover, for human administration, preparations will of course preferably meet sterility, pyrogenicity, and the general safety and purity  
20 standards as required by FDA Office of Biologics standards.

In another embodiment of the invention, the compositions disclosed herein may be formulated in a neutral or salt form. Illustrative pharmaceutically-acceptable salts include the acid addition salts (formed with the free amino groups of the protein) and which are formed with inorganic acids such as, for  
25 example, hydrochloric or phosphoric acids, or such organic acids as acetic, oxalic, tartaric, mandelic, and the like. Salts formed with the free carboxyl groups can also be derived from inorganic bases such as, for example, sodium, potassium, ammonium, calcium, or ferric hydroxides, and such organic bases as isopropylamine, trimethylamine, histidine, procaine and the like. Upon formulation, solutions will be

administered in a manner compatible with the dosage formulation and in such amount as is therapeutically effective.

The carriers can further comprise any and all solvents, dispersion media, vehicles, coatings, diluents, antibacterial and antifungal agents, isotonic and absorption  
5 delaying agents, buffers, carrier solutions, suspensions, colloids, and the like. The use of such media and agents for pharmaceutical active substances is well known in the art. Except insofar as any conventional media or agent is incompatible with the active ingredient, its use in the therapeutic compositions is contemplated. Supplementary active ingredients can also be incorporated into the compositions. The phrase  
10 "pharmaceutically-acceptable" refers to molecular entities and compositions that do not produce an allergic or similar untoward reaction when administered to a human.

In certain embodiments, the pharmaceutical compositions may be delivered by intranasal sprays, inhalation, and/or other aerosol delivery vehicles. Methods for delivering genes, nucleic acids, and peptide compositions directly to the  
15 lungs *via* nasal aerosol sprays has been described, *e.g.*, in U. S. Patent 5,756,353 and U. S. Patent 5,804,212. Likewise, the delivery of drugs using intranasal microparticle resins (Takenaga *et al.*, J Controlled Release 1998 Mar 2;52(1-2):81-7) and lysophosphatidyl-glycerol compounds (U. S. Patent 5,725,871) are also well-known in the pharmaceutical arts. Likewise, illustrative transmucosal drug delivery in the form of  
20 a polytetrafluoroethylene support matrix is described in U. S. Patent 5,780,045.

In certain embodiments, liposomes, nanocapsules, microparticles, lipid particles, vesicles, and the like, are used for the introduction of the compositions of the present invention into suitable host cells/organisms. In particular, the compositions of the present invention may be formulated for delivery either encapsulated in a lipid  
25 particle, a liposome, a vesicle, a nanosphere, or a nanoparticle or the like. Alternatively, compositions of the present invention can be bound, either covalently or non-covalently, to the surface of such carrier vehicles.

The formation and use of liposome and liposome-like preparations as potential drug carriers is generally known to those of skill in the art (see for example,  
30 Lasic, Trends Biotechnol 1998 Jul;16(7):307-21; Takakura, Nippon Rinsho 1998

Mar;56(3):691-5; Chandran *et al.*, Indian J Exp Biol. 1997 Aug;35(8):801-9; Margalit, Crit Rev Ther Drug Carrier Syst. 1995;12(2-3):233-61; U.S. Patent 5,567,434; U.S. Patent 5,552,157; U.S. Patent 5,565,213; U.S. Patent 5,738,868 and U.S. Patent 5,795,587, each specifically incorporated herein by reference in its entirety).

5               Liposomes have been used successfully with a number of cell types that are normally difficult to transfect by other procedures, including T cell suspensions, primary hepatocyte cultures and PC 12 cells (Renneisen *et al.*, J Biol Chem. 1990 Sep 25;265(27):16337-42; Muller *et al.*, DNA Cell Biol. 1990 Apr;9(3):221-9). In addition, liposomes are free of the DNA length constraints that are typical of viral-based delivery  
10 systems. Liposomes have been used effectively to introduce genes, various drugs, radiotherapeutic agents, enzymes, viruses, transcription factors, allosteric effectors and the like, into a variety of cultured cell lines and animals. Furthermore, the use of liposomes does not appear to be associated with autoimmune responses or unacceptable toxicity after systemic delivery.

15               In certain embodiments, liposomes are formed from phospholipids that are dispersed in an aqueous medium and spontaneously form multilamellar concentric bilayer vesicles (also termed multilamellar vesicles (MLVs)).

              Alternatively, in other embodiments, the invention provides for pharmaceutically-acceptable nanocapsule formulations of the compositions of the  
20 present invention. Nanocapsules can generally entrap compounds in a stable and reproducible way (see, for example, Quintanar-Guerrero *et al.*, Drug Dev Ind Pharm. 1998 Dec;24(12):1113-28). To avoid side effects due to intracellular polymeric overloading, such ultrafine particles (sized around 0.1  $\mu\text{m}$ ) may be designed using polymers able to be degraded *in vivo*. Such particles can be made as described, for  
25 example, by Couvreur *et al.*, Crit Rev Ther Drug Carrier Syst. 1988;5(1):1-20; zur Muhlen *et al.*, Eur J Pharm Biopharm. 1998 Mar;45(2):149-55; Zambaux *et al.* J Controlled Release. 1998 Jan 2;50(1-3):31-40; and U. S. Patent 5,145,684.

Cancer Therapeutic Methods

In further aspects of the present invention, the pharmaceutical compositions described herein may be used for the treatment of cancer, particularly for the immunotherapy of prostate cancer. Within such methods, the pharmaceutical compositions described herein are administered to a patient, typically a warm-blooded animal, preferably a human. A patient may or may not be afflicted with cancer. Accordingly, the above pharmaceutical compositions may be used to prevent the development of a cancer or to treat a patient afflicted with a cancer. Pharmaceutical compositions and vaccines may be administered either prior to or following surgical removal of primary tumors and/or treatment such as administration of radiotherapy or conventional chemotherapeutic drugs. As discussed above, administration of the pharmaceutical compositions may be by any suitable method, including administration by intravenous, intraperitoneal, intramuscular, subcutaneous, intranasal, intradermal, anal, vaginal, topical and oral routes.

Within certain embodiments, immunotherapy may be active immunotherapy, in which treatment relies on the *in vivo* stimulation of the endogenous host immune system to react against tumors with the administration of immune response-modifying agents (such as polypeptides and polynucleotides as provided herein).

Within other embodiments, immunotherapy may be passive immunotherapy, in which treatment involves the delivery of agents with established tumor-immune reactivity (such as effector cells or antibodies) that can directly or indirectly mediate antitumor effects and does not necessarily depend on an intact host immune system. Examples of effector cells include T cells as discussed above, T lymphocytes (such as CD8<sup>+</sup> cytotoxic T lymphocytes and CD4<sup>+</sup> T-helper tumor-infiltrating lymphocytes), killer cells (such as Natural Killer cells and lymphokine-activated killer cells), B cells and antigen-presenting cells (such as dendritic cells and macrophages) expressing a polypeptide provided herein. T cell receptors and antibody receptors specific for the polypeptides recited herein may be cloned, expressed and transferred into other vectors or effector cells for adoptive immunotherapy. The

polypeptides provided herein may also be used to generate antibodies or anti-idiotypic antibodies (as described above and in U.S. Patent No. 4,918,164) for passive immunotherapy.

Effector cells may generally be obtained in sufficient quantities for adoptive immunotherapy by growth *in vitro*, as described herein. Culture conditions for expanding single antigen-specific effector cells to several billion in number with retention of antigen recognition *in vivo* are well known in the art. Such *in vitro* culture conditions typically use intermittent stimulation with antigen, often in the presence of cytokines (such as IL-2) and non-dividing feeder cells. As noted above, immunoreactive polypeptides as provided herein may be used to rapidly expand antigen-specific T cell cultures in order to generate a sufficient number of cells for immunotherapy. In particular, antigen-presenting cells, such as dendritic, macrophage, monocyte, fibroblast and/or B cells, may be pulsed with immunoreactive polypeptides or transfected with one or more polynucleotides using standard techniques well known in the art. For example, antigen-presenting cells can be transfected with a polynucleotide having a promoter appropriate for increasing expression in a recombinant virus or other expression system. Cultured effector cells for use in therapy must be able to grow and distribute widely, and to survive long term *in vivo*. Studies have shown that cultured effector cells can be induced to grow *in vivo* and to survive long term in substantial numbers by repeated stimulation with antigen supplemented with IL-2 (*see, for example, Cheever et al., Immunological Reviews 157:177, 1997*).

Alternatively, a vector expressing a polypeptide recited herein may be introduced into antigen presenting cells taken from a patient and clonally propagated *ex vivo* for transplant back into the same patient. Transfected cells may be reintroduced into the patient using any means known in the art, preferably in sterile form by intravenous, intracavitary, intraperitoneal or intratumor administration.

Routes and frequency of administration of the therapeutic compositions described herein, as well as dosage, will vary from individual to individual, and may be readily established using standard techniques. In general, the pharmaceutical compositions and vaccines may be administered by injection (*e.g., intracutaneous,*

intramuscular, intravenous or subcutaneous), intranasally (*e.g.*, by aspiration) or orally. Preferably, between 1 and 10 doses may be administered over a 52 week period. Preferably, 6 doses are administered, at intervals of 1 month, and booster vaccinations may be given periodically thereafter. Alternate protocols may be appropriate for individual patients. A suitable dose is an amount of a compound that, when administered as described above, is capable of promoting an anti-tumor immune response, and is at least 10-50% above the basal (*i.e.*, untreated) level. Such response can be monitored by measuring the anti-tumor antibodies in a patient or by vaccine-dependent generation of cytolytic effector cells capable of killing the patient's tumor cells *in vitro*. Such vaccines should also be capable of causing an immune response that leads to an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial or longer disease-free survival) in vaccinated patients as compared to non-vaccinated patients. In general, for pharmaceutical compositions and vaccines comprising one or more polypeptides, the amount of each polypeptide present in a dose ranges from about 25  $\mu$ g to 5 mg per kg of host. Suitable dose sizes will vary with the size of the patient, but will typically range from about 0.1 mL to about 5 mL.

In general, an appropriate dosage and treatment regimen provides the active compound(s) in an amount sufficient to provide therapeutic and/or prophylactic benefit. Such a response can be monitored by establishing an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial, or longer disease-free survival) in treated patients as compared to non-treated patients. Increases in preexisting immune responses to a tumor protein generally correlate with an improved clinical outcome. Such immune responses may generally be evaluated using standard proliferation, cytotoxicity or cytokine assays, which may be performed using samples obtained from a patient before and after treatment.

#### Cancer Detection and Diagnostic Compositions, Methods and Kits

In general, a cancer may be detected in a patient based on the presence of one or more prostate tumor proteins and/or polynucleotides encoding such proteins in a biological sample (for example, blood, sera, sputum urine and/or tumor biopsies)

obtained from the patient. In other words, such proteins may be used as markers to indicate the presence or absence of a cancer such as prostate cancer. In addition, such proteins may be useful for the detection of other cancers. The binding agents provided herein generally permit detection of the level of antigen that binds to the agent in the biological sample. Polynucleotide primers and probes may be used to detect the level of mRNA encoding a tumor protein, which is also indicative of the presence or absence of a cancer. In general, a prostate tumor sequence should be present at a level that is at least three fold higher in tumor tissue than in normal tissue

There are a variety of assay formats known to those of ordinary skill in the art for using a binding agent to detect polypeptide markers in a sample. *See, e.g.,* Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, the presence or absence of a cancer in a patient may be determined by (a) contacting a biological sample obtained from a patient with a binding agent; (b) detecting in the sample a level of polypeptide that binds to the binding agent; and (c) comparing the level of polypeptide with a predetermined cut-off value.

In a preferred embodiment, the assay involves the use of binding agent immobilized on a solid support to bind to and remove the polypeptide from the remainder of the sample. The bound polypeptide may then be detected using a detection reagent that contains a reporter group and specifically binds to the binding agent/polypeptide complex. Such detection reagents may comprise, for example, a binding agent that specifically binds to the polypeptide or an antibody or other agent that specifically binds to the binding agent, such as an anti-immunoglobulin, protein G, protein A or a lectin. Alternatively, a competitive assay may be utilized, in which a polypeptide is labeled with a reporter group and allowed to bind to the immobilized binding agent after incubation of the binding agent with the sample. The extent to which components of the sample inhibit the binding of the labeled polypeptide to the binding agent is indicative of the reactivity of the sample with the immobilized binding agent. Suitable polypeptides for use within such assays include full length prostate tumor proteins and polypeptide portions thereof to which the binding agent binds, as described above.



The solid support may be any material known to those of ordinary skill in the art to which the tumor protein may be attached. For example, the solid support may be a test well in a microtiter plate or a nitrocellulose or other suitable membrane. Alternatively, the support may be a bead or disc, such as glass, fiberglass, latex or a plastic material such as polystyrene or polyvinylchloride. The support may also be a magnetic particle or a fiber optic sensor, such as those disclosed, for example, in U.S. Patent No. 5,359,681. The binding agent may be immobilized on the solid support using a variety of techniques known to those of skill in the art, which are amply described in the patent and scientific literature. In the context of the present invention, the term "immobilization" refers to both noncovalent association, such as adsorption, and covalent attachment (which may be a direct linkage between the agent and functional groups on the support or may be a linkage by way of a cross-linking agent). Immobilization by adsorption to a well in a microtiter plate or to a membrane is preferred. In such cases, adsorption may be achieved by contacting the binding agent, in a suitable buffer, with the solid support for a suitable amount of time. The contact time varies with temperature, but is typically between about 1 hour and about 1 day. In general, contacting a well of a plastic microtiter plate (such as polystyrene or polyvinylchloride) with an amount of binding agent ranging from about 10 ng to about 10  $\mu$ g, and preferably about 100 ng to about 1  $\mu$ g, is sufficient to immobilize an adequate amount of binding agent.

Covalent attachment of binding agent to a solid support may generally be achieved by first reacting the support with a bifunctional reagent that will react with both the support and a functional group, such as a hydroxyl or amino group, on the binding agent. For example, the binding agent may be covalently attached to supports having an appropriate polymer coating using benzoquinone or by condensation of an aldehyde group on the support with an amine and an active hydrogen on the binding partner (*see, e.g.,* Pierce Immunotechnology Catalog and Handbook, 1991, at A12-A13).

In certain embodiments, the assay is a two-antibody sandwich assay. This assay may be performed by first contacting an antibody that has been immobilized

on a solid support, commonly the well of a microtiter plate, with the sample, such that polypeptides within the sample are allowed to bind to the immobilized antibody. Unbound sample is then removed from the immobilized polypeptide-antibody complexes and a detection reagent (preferably a second antibody capable of binding to a different site on the polypeptide) containing a reporter group is added. The amount of detection reagent that remains bound to the solid support is then determined using a method appropriate for the specific reporter group.

More specifically, once the antibody is immobilized on the support as described above, the remaining protein binding sites on the support are typically blocked. Any suitable blocking agent known to those of ordinary skill in the art, such as bovine serum albumin or Tween 20™ (Sigma Chemical Co., St. Louis, MO). The immobilized antibody is then incubated with the sample, and polypeptide is allowed to bind to the antibody. The sample may be diluted with a suitable diluent, such as phosphate-buffered saline (PBS) prior to incubation. In general, an appropriate contact time (*i.e.*, incubation time) is a period of time that is sufficient to detect the presence of polypeptide within a sample obtained from an individual with prostate cancer. Preferably, the contact time is sufficient to achieve a level of binding that is at least about 95% of that achieved at equilibrium between bound and unbound polypeptide. Those of ordinary skill in the art will recognize that the time necessary to achieve equilibrium may be readily determined by assaying the level of binding that occurs over a period of time. At room temperature, an incubation time of about 30 minutes is generally sufficient.

Unbound sample may then be removed by washing the solid support with an appropriate buffer, such as PBS containing 0.1% Tween 20™. The second antibody, which contains a reporter group, may then be added to the solid support. Preferred reporter groups include those groups recited above.

The detection reagent is then incubated with the immobilized antibody-polypeptide complex for an amount of time sufficient to detect the bound polypeptide. An appropriate amount of time may generally be determined by assaying the level of binding that occurs over a period of time. Unbound detection reagent is then removed

and bound detection reagent is detected using the reporter group. The method employed for detecting the reporter group depends upon the nature of the reporter group. For radioactive groups, scintillation counting or autoradiographic methods are generally appropriate. Spectroscopic methods may be used to detect dyes, luminescent groups and fluorescent groups. Biotin may be detected using avidin, coupled to a different reporter group (commonly a radioactive or fluorescent group or an enzyme). Enzyme reporter groups may generally be detected by the addition of substrate (generally for a specific period of time), followed by spectroscopic or other analysis of the reaction products.

10 To determine the presence or absence of a cancer, such as prostate cancer, the signal detected from the reporter group that remains bound to the solid support is generally compared to a signal that corresponds to a predetermined cut-off value. In one preferred embodiment, the cut-off value for the detection of a cancer is the average mean signal obtained when the immobilized antibody is incubated with  
15 samples from patients without the cancer. In general, a sample generating a signal that is three standard deviations above the predetermined cut-off value is considered positive for the cancer. In an alternate preferred embodiment, the cut-off value is determined using a Receiver Operator Curve, according to the method of Sackett et al., *Clinical Epidemiology: A Basic Science for Clinical Medicine*, Little Brown and Co., 1985,  
20 p. 106-7. Briefly, in this embodiment, the cut-off value may be determined from a plot of pairs of true positive rates (*i.e.*, sensitivity) and false positive rates (100%-specificity) that correspond to each possible cut-off value for the diagnostic test result. The cut-off value on the plot that is the closest to the upper left-hand corner (*i.e.*, the value that encloses the largest area) is the most accurate cut-off value, and a sample generating a  
25 signal that is higher than the cut-off value determined by this method may be considered positive. Alternatively, the cut-off value may be shifted to the left along the plot, to minimize the false positive rate, or to the right, to minimize the false negative rate. In general, a sample generating a signal that is higher than the cut-off value determined by this method is considered positive for a cancer.

In a related embodiment, the assay is performed in a flow-through or strip test format, wherein the binding agent is immobilized on a membrane, such as nitrocellulose. In the flow-through test, polypeptides within the sample bind to the immobilized binding agent as the sample passes through the membrane. A second, labeled binding agent then binds to the binding agent-polypeptide complex as a solution containing the second binding agent flows through the membrane. The detection of bound second binding agent may then be performed as described above. In the strip test format, one end of the membrane to which binding agent is bound is immersed in a solution containing the sample. The sample migrates along the membrane through a region containing second binding agent and to the area of immobilized binding agent. Concentration of second binding agent at the area of immobilized antibody indicates the presence of a cancer. Typically, the concentration of second binding agent at that site generates a pattern, such as a line, that can be read visually. The absence of such a pattern indicates a negative result. In general, the amount of binding agent immobilized on the membrane is selected to generate a visually discernible pattern when the biological sample contains a level of polypeptide that would be sufficient to generate a positive signal in the two-antibody sandwich assay, in the format discussed above. Preferred binding agents for use in such assays are antibodies and antigen-binding fragments thereof. Preferably, the amount of antibody immobilized on the membrane ranges from about 25 ng to about 1  $\mu$ g, and more preferably from about 50 ng to about 500 ng. Such tests can typically be performed with a very small amount of biological sample.

Of course, numerous other assay protocols exist that are suitable for use with the tumor proteins or binding agents of the present invention. The above descriptions are intended to be exemplary only. For example, it will be apparent to those of ordinary skill in the art that the above protocols may be readily modified to use tumor polypeptides to detect antibodies that bind to such polypeptides in a biological sample. The detection of such tumor protein specific antibodies may correlate with the presence of a cancer.

A cancer may also, or alternatively, be detected based on the presence of T cells that specifically react with a tumor protein in a biological sample. Within certain methods, a biological sample comprising CD4<sup>+</sup> and/or CD8<sup>+</sup> T cells isolated from a patient is incubated with a tumor polypeptide, a polynucleotide encoding such a polypeptide and/or an APC that expresses at least an immunogenic portion of such a polypeptide, and the presence or absence of specific activation of the T cells is detected. Suitable biological samples include, but are not limited to, isolated T cells. For example, T cells may be isolated from a patient by routine techniques (such as by Ficoll/Hypaque density gradient centrifugation of peripheral blood lymphocytes). T cells may be incubated *in vitro* for 2-9 days (typically 4 days) at 37°C with polypeptide (e.g., 5 - 25 µg/ml). It may be desirable to incubate another aliquot of a T cell sample in the absence of tumor polypeptide to serve as a control. For CD4<sup>+</sup> T cells, activation is preferably detected by evaluating proliferation of the T cells. For CD8<sup>+</sup> T cells, activation is preferably detected by evaluating cytolytic activity. A level of proliferation that is at least two fold greater and/or a level of cytolytic activity that is at least 20% greater than in disease-free patients indicates the presence of a cancer in the patient.

As noted above, a cancer may also, or alternatively, be detected based on the level of mRNA encoding a tumor protein in a biological sample. For example, at least two oligonucleotide primers may be employed in a polymerase chain reaction (PCR) based assay to amplify a portion of a tumor cDNA derived from a biological sample, wherein at least one of the oligonucleotide primers is specific for (*i.e.*, hybridizes to) a polynucleotide encoding the tumor protein. The amplified cDNA is then separated and detected using techniques well known in the art, such as gel electrophoresis. Similarly, oligonucleotide probes that specifically hybridize to a polynucleotide encoding a tumor protein may be used in a hybridization assay to detect the presence of polynucleotide encoding the tumor protein in a biological sample.

To permit hybridization under assay conditions, oligonucleotide primers and probes should comprise an oligonucleotide sequence that has at least about 60%, preferably at least about 75% and more preferably at least about 90%, identity to a portion of a polynucleotide encoding a tumor protein of the invention that is at least 10

nucleotides, and preferably at least 20 nucleotides, in length. Preferably, oligonucleotide primers and/or probes hybridize to a polynucleotide encoding a polypeptide described herein under moderately stringent conditions, as defined above. Oligonucleotide primers and/or probes which may be usefully employed in the diagnostic methods described herein preferably are at least 10-40 nucleotides in length. In a preferred embodiment, the oligonucleotide primers comprise at least 10 contiguous nucleotides, more preferably at least 15 contiguous nucleotides, of a DNA molecule having a sequence as disclosed herein. Techniques for both PCR based assays and hybridization assays are well known in the art (*see*, for example, Mullis et al., *Cold Spring Harbor Symp. Quant. Biol.*, 51:263, 1987; Erlich ed., *PCR Technology*, Stockton Press, NY, 1989).

One preferred assay employs RT-PCR, in which PCR is applied in conjunction with reverse transcription. Typically, RNA is extracted from a biological sample, such as biopsy tissue, and is reverse transcribed to produce cDNA molecules. PCR amplification using at least one specific primer generates a cDNA molecule, which may be separated and visualized using, for example, gel electrophoresis. Amplification may be performed on biological samples taken from a test patient and from an individual who is not afflicted with a cancer. The amplification reaction may be performed on several dilutions of cDNA spanning two orders of magnitude. A two-fold or greater increase in expression in several dilutions of the test patient sample as compared to the same dilutions of the non-cancerous sample is typically considered positive.

In another embodiment, the compositions described herein may be used as markers for the progression of cancer. In this embodiment, assays as described above for the diagnosis of a cancer may be performed over time, and the change in the level of reactive polypeptide(s) or polynucleotide(s) evaluated. For example, the assays may be performed every 24-72 hours for a period of 6 months to 1 year, and thereafter performed as needed. In general, a cancer is progressing in those patients in whom the level of polypeptide or polynucleotide detected increases over time. In contrast, the

cancer is not progressing when the level of reactive polypeptide or polynucleotide either remains constant or decreases with time.

Certain *in vivo* diagnostic assays may be performed directly on a tumor. One such assay involves contacting tumor cells with a binding agent. The bound  
5 binding agent may then be detected directly or indirectly via a reporter group. Such binding agents may also be used in histological applications. Alternatively, polynucleotide probes may be used within such applications.

As noted above, to improve sensitivity, multiple tumor protein markers may be assayed within a given sample. It will be apparent that binding agents specific  
10 for different proteins provided herein may be combined within a single assay. Further, multiple primers or probes may be used concurrently. The selection of tumor protein markers may be based on routine experiments to determine combinations that results in optimal sensitivity. In addition, or alternatively, assays for tumor proteins provided herein may be combined with assays for other known tumor antigens.

15 The present invention further provides kits for use within any of the above diagnostic methods. Such kits typically comprise two or more components necessary for performing a diagnostic assay. Components may be compounds, reagents, containers and/or equipment. For example, one container within a kit may contain a monoclonal antibody or fragment thereof that specifically binds to a tumor protein.  
20 Such antibodies or fragments may be provided attached to a support material, as described above. One or more additional containers may enclose elements, such as reagents or buffers, to be used in the assay. Such kits may also, or alternatively, contain a detection reagent as described above that contains a reporter group suitable for direct or indirect detection of antibody binding.

25 Alternatively, a kit may be designed to detect the level of mRNA encoding a tumor protein in a biological sample. Such kits generally comprise at least one oligonucleotide probe or primer, as described above, that hybridizes to a polynucleotide encoding a tumor protein. Such an oligonucleotide may be used, for example, within a PCR or hybridization assay. Additional components that may be

present within such kits include a second oligonucleotide and/or a diagnostic reagent or container to facilitate the detection of a polynucleotide encoding a tumor protein.

The following Examples are offered by way of illustration and not by way of limitation.



EXAMPLES

## EXAMPLE 1

## 5 ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC POLYPEPTIDES

This Example describes the isolation of certain prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library was constructed from  
10 prostate tumor poly A<sup>+</sup> RNA using a Superscript Plasmid System for cDNA Synthesis and Plasmid Cloning kit (BRL Life Technologies, Gaithersburg, MD 20897) following the manufacturer's protocol. Specifically, prostate tumor tissues were homogenized with polytron (Kinematica, Switzerland) and total RNA was extracted using Trizol reagent (BRL Life Technologies) as directed by the manufacturer. The poly A<sup>+</sup> RNA  
15 was then purified using a Qiagen oligotex spin column mRNA purification kit (Qiagen, Santa Clarita, CA 91355) according to the manufacturer's protocol. First-strand cDNA was synthesized using the NotI/Oligo-dT18 primer. Double-stranded cDNA was synthesized, ligated with EcoRI/BAXI adaptors (Invitrogen, San Diego, CA) and digested with NotI. Following size fractionation with Chroma Spin-1000 columns  
20 (Clontech, Palo Alto, CA), the cDNA was ligated into the EcoRI/NotI site of pCDNA3.1 (Invitrogen) and transformed into ElectroMax *E. coli* DH10B cells (BRL Life Technologies) by electroporation.

Using the same procedure, a normal human pancreas cDNA expression library was prepared from a pool of six tissue specimens (Clontech). The cDNA  
25 libraries were characterized by determining the number of independent colonies, the percentage of clones that carried insert, the average insert size and by sequence analysis. The prostate tumor library contained  $1.64 \times 10^7$  independent colonies, with 70% of clones having an insert and the average insert size being 1745 base pairs. The normal pancreas cDNA library contained  $3.3 \times 10^6$  independent colonies, with 69% of clones  
30 having inserts and the average insert size being 1120 base pairs. For both libraries,

sequence analysis showed that the majority of clones had a full length cDNA sequence and were synthesized from mRNA, with minimal rRNA and mitochondrial DNA contamination.

cDNA library subtraction was performed using the above prostate tumor and normal pancreas cDNA libraries, as described by Hara *et al.* (*Blood*, 84:189-199, 1994) with some modifications. Specifically, a prostate tumor-specific subtracted cDNA library was generated as follows. Normal pancreas cDNA library (70 µg) was digested with EcoRI, NotI, and SfuI, followed by a filling-in reaction with DNA polymerase Klenow fragment. After phenol-chloroform extraction and ethanol precipitation, the DNA was dissolved in 100 µl of H<sub>2</sub>O, heat-denatured and mixed with 100 µl (100 µg) of Photoprobe biotin (Vector Laboratories, Burlingame, CA). As recommended by the manufacturer, the resulting mixture was irradiated with a 270 W sunlamp on ice for 20 minutes. Additional Photoprobe biotin (50 µl) was added and the biotinylation reaction was repeated. After extraction with butanol five times, the DNA was ethanol-precipitated and dissolved in 23 µl H<sub>2</sub>O to form the driver DNA.

To form the tracer DNA, 10 µg prostate tumor cDNA library was digested with BamHI and XhoI, phenol chloroform extracted and passed through Chroma spin-400 columns (Clontech). Following ethanol precipitation, the tracer DNA was dissolved in 5 µl H<sub>2</sub>O. Tracer DNA was mixed with 15 µl driver DNA and 20 µl of 2 x hybridization buffer (1.5 M NaCl/10 mM EDTA/50 mM HEPES pH 7.5/0.2% sodium dodecyl sulfate), overlaid with mineral oil, and heat-denatured completely. The sample was immediately transferred into a 68 °C water bath and incubated for 20 hours (long hybridization [LH]). The reaction mixture was then subjected to a streptavidin treatment followed by phenol/chloroform extraction. This process was repeated three more times. Subtracted DNA was precipitated, dissolved in 12 µl H<sub>2</sub>O, mixed with 8 µl driver DNA and 20 µl of 2 x hybridization buffer, and subjected to a hybridization at 68 °C for 2 hours (short hybridization [SH]). After removal of biotinylated double-stranded DNA, subtracted cDNA was ligated into BamHI/XhoI site of chloramphenicol resistant pBCSK<sup>+</sup> (Stratagene, La Jolla, CA 92037) and transformed into ElectroMax *E.*

*coli* DH10B cells by electroporation to generate a prostate tumor specific subtracted cDNA library (referred to as "prostate subtraction 1").

To analyze the subtracted cDNA library, plasmid DNA was prepared from 100 independent clones, randomly picked from the subtracted prostate tumor specific library and grouped based on insert size. Representative cDNA clones were further characterized by DNA sequencing with a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A (Foster City, CA). Six cDNA clones, hereinafter referred to as F1-13, F1-12, F1-16, H1-1, H1-9 and H1-4, were shown to be abundant in the subtracted prostate-specific cDNA library. The determined 3' and 5' cDNA sequences for F1-12 are provided in SEQ ID NO: 2 and 3, respectively, with determined 3' cDNA sequences for F1-13, F1-16, H1-1, H1-9 and H1-4 being provided in SEQ ID NO: 1 and 4-7, respectively.

The cDNA sequences for the isolated clones were compared to known sequences in the gene bank using the EMBL and GenBank databases (release 96). Four of the prostate tumor cDNA clones, F1-13, F1-16, H1-1, and H1-4, were determined to encode the following previously identified proteins: prostate specific antigen (PSA), human glandular kallikrein, human tumor expression enhanced gene, and mitochondria cytochrome C oxidase subunit II. H1-9 was found to be identical to a previously identified human autonomously replicating sequence. No significant homologies to the cDNA sequence for F1-12 were found.

Subsequent studies led to the isolation of a full-length cDNA sequence for F1-12 (also referred to as P504S). This sequence is provided in SEQ ID NO: 107, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 108. cDNA splice variants of P504S are provided in SEQ ID NO: 600-605.

To clone less abundant prostate tumor specific genes, cDNA library subtraction was performed by subtracting the prostate tumor cDNA library described above with the normal pancreas cDNA library and with the three most abundant genes in the previously subtracted prostate tumor specific cDNA library: human glandular kallikrein, prostate specific antigen (PSA), and mitochondria cytochrome C oxidase subunit II. Specifically, 1  $\mu$ g each of human glandular kallikrein, PSA and

mitochondria cytochrome C oxidase subunit II cDNAs in pCDNA3.1 were added to the driver DNA and subtraction was performed as described above to provide a second subtracted cDNA library hereinafter referred to as the "subtracted prostate tumor specific cDNA library with spike".

5                   Twenty-two cDNA clones were isolated from the subtracted prostate tumor specific cDNA library with spike. The determined 3' and 5' cDNA sequences for the clones referred to as J1-17, L1-12, N1-1862, J1-13, J1-19, J1-25, J1-24, K1-58, K1-63, L1-4 and L1-14 are provided in SEQ ID NOS: 8-9, 10-11, 12-13, 14-15, 16-17, 18-19, 20-21, 22-23, 24-25, 26-27 and 28-29, respectively. The determined 3' cDNA  
10 sequences for the clones referred to as J1-12, J1-16, J1-21, K1-48, K1-55, L1-2, L1-6, N1-1858, N1-1860, N1-1861, N1-1864 are provided in SEQ ID NOS: 30-40, respectively. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to three of the five most abundant DNA species, (J1-17, L1-12 and N1-1862; SEQ ID NOS: 8-9, 10-11 and 12-13, respectively).  
15 Of the remaining two most abundant species, one (J1-12; SEQ ID NO:30) was found to be identical to the previously identified human pulmonary surfactant-associated protein, and the other (K1-48; SEQ ID NO:33) was determined to have some homology to *R. norvegicus* mRNA for 2-arylpropionyl-CoA epimerase. Of the 17 less abundant cDNA clones isolated from the subtracted prostate tumor specific cDNA library with spike,  
20 four (J1-16, K1-55, L1-6 and N1-1864; SEQ ID NOS:31, 34, 36 and 40, respectively) were found to be identical to previously identified sequences, two (J1-21 and N1-1860; SEQ ID NOS: 32 and 38, respectively) were found to show some homology to non-human sequences, and two (L1-2 and N1-1861; SEQ ID NOS: 35 and 39, respectively) were found to show some homology to known human sequences. No significant  
25 homologies were found to the polypeptides J1-13, J1-19, J1-24, J1-25, K1-58, K1-63, L1-4, L1-14 (SEQ ID NOS: 14-15, 16-17, 20-21, 18-19, 22-23, 24-25, 26-27, 28-29, respectively).

Subsequent studies led to the isolation of full length cDNA sequences for J1-17, L1-12 and N1-1862 (SEQ ID NOS: 109-111, respectively). The corresponding

predicted amino acid sequences are provided in SEQ ID NOS: 112-114. L1-12 is also referred to as P501S. A cDNA splice variant of P501S is provided in SEQ ID NO: 606.

In a further experiment, four additional clones were identified by subtracting a prostate tumor cDNA library with normal prostate cDNA prepared from a pool of three normal prostate poly A+ RNA (referred to as "prostate subtraction 2"). The determined cDNA sequences for these clones, hereinafter referred to as U1-3064, U1-3065, V1-3692 and 1A-3905, are provided in SEQ ID NO: 69-72, respectively. Comparison of the determined sequences with those in the gene bank revealed no significant homologies to U1-3065.

A second subtraction with spike (referred to as "prostate subtraction spike 2") was performed by subtracting a prostate tumor specific cDNA library with spike with normal pancreas cDNA library and further spiked with PSA, J1-17, pulmonary surfactant-associated protein, mitochondrial DNA, cytochrome c oxidase subunit II, N1-1862, autonomously replicating sequence, L1-12 and tumor expression enhanced gene. Four additional clones, hereinafter referred to as V1-3686, R1-2330, 1B-3976 and V1-3679, were isolated. The determined cDNA sequences for these clones are provided in SEQ ID NO:73-76, respectively. Comparison of these sequences with those in the gene bank revealed no significant homologies to V1-3686 and R1-2330.

Further analysis of the three prostate subtractions described above (prostate subtraction 2, subtracted prostate tumor specific cDNA library with spike, and prostate subtraction spike 2) resulted in the identification of sixteen additional clones, referred to as 1G-4736, 1G-4738, 1G-4741, 1G-4744, 1G-4734, 1H-4774, 1H-4781, 1H-4785, 1H-4787, 1H-4796, 1I-4810, 1I-4811, 1J-4876, 1K-4884 and 1K-4896. The determined cDNA sequences for these clones are provided in SEQ ID NOS: 77-92, respectively. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to 1G-4741, 1G-4734, 1I-4807, 1J-4876 and 1K-4896 (SEQ ID NOS: 79, 81, 87, 90 and 92, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1G-4736, 1G-4738, 1G-4741, 1G-4744, 1H-4774, 1H-4781, 1H-4785, 1H-4787, 1H-4796, 1I-4807,

1J-4876, 1K-4884 and 1K-4896, provided in SEQ ID NOS: 179-188 and 191-193, respectively, and to the determination of additional partial cDNA sequences for 1I-4810 and 1I-4811, provided in SEQ ID NOS: 189 and 190, respectively.

Additional studies with prostate subtraction spike 2 resulted in the  
5 isolation of three more clones. Their sequences were determined as described above and compared to the most recent GenBank. All three clones were found to have homology to known genes, which are Cysteine-rich protein, KIAA0242, and KIAA0280 (SEQ ID NO: 317, 319, and 320, respectively). Further analysis of these clones by Synteni microarray (Synteni, Palo Alto, CA) demonstrated that all three clones were  
10 over-expressed in most prostate tumors and prostate BPH, as well as in the majority of normal prostate tissues tested, but low expression in all other normal tissues.

An additional subtraction was performed by subtracting a normal prostate cDNA library with normal pancreas cDNA (referred to as "prostate subtraction 3"). This led to the identification of six additional clones referred to as 1G-4761, 1G-  
15 4762, 1H-4766, 1H-4770, 1H-4771 and 1H-4772 (SEQ ID NOS: 93-98). Comparison of these sequences with those in the gene bank revealed no significant homologies to 1G-4761 and 1H-4771 (SEQ ID NOS: 93 and 97, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1G-4761, 1G-4762, 1H-4766 and 1H-4772 provided in SEQ ID NOS: 194-196 and 199, respectively,  
20 and to the determination of additional partial cDNA sequences for 1H-4770 and 1H-4771, provided in SEQ ID NOS: 197 and 198, respectively.

Subtraction of a prostate tumor cDNA library, prepared from a pool of polyA<sup>+</sup> RNA from three prostate cancer patients, with a normal pancreas cDNA library (prostate subtraction 4) led to the identification of eight clones, referred to as 1D-4297,  
25 1D-4309, 1D.1-4278, 1D-4288, 1D-4283, 1D-4304, 1D-4296 and 1D-4280 (SEQ ID NOS: 99-107). These sequences were compared to those in the gene bank as described above. No significant homologies were found to 1D-4283 and 1D-4304 (SEQ ID NOS: 103 and 104, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1D-4309, 1D.1-4278, 1D-4288, 1D-

4283, 1D-4304, 1D-4296 and 1D-4280, provided in SEQ ID NOS: 200-206, respectively.

cDNA clones isolated in prostate subtraction 1 and prostate subtraction 2, described above, were colony PCR amplified and their mRNA expression levels in prostate tumor, normal prostate and in various other normal tissues were determined using microarray technology (Synteni, Palo Alto, CA). Briefly, the PCR amplification products were dotted onto slides in an array format, with each product occupying a unique location in the array. mRNA was extracted from the tissue sample to be tested, reverse transcribed, and fluorescent-labeled cDNA probes were generated. The microarrays were probed with the labeled cDNA probes, the slides scanned and fluorescence intensity was measured. This intensity correlates with the hybridization intensity. Two clones (referred to as P509S and P510S) were found to be over-expressed in prostate tumor and normal prostate and expressed at low levels in all other normal tissues tested (liver, pancreas, skin, bone marrow, brain, breast, adrenal gland, bladder, testes, salivary gland, large intestine, kidney, ovary, lung, spinal cord, skeletal muscle and colon). The determined cDNA sequences for P509S and P510S are provided in SEQ ID NO: 223 and 224, respectively. Comparison of these sequences with those in the gene bank as described above, revealed some homology to previously identified ESTs.

Additional studies led to the isolation of the full-length cDNA sequence for P509S. This sequence is provided in SEQ ID NO: 332, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 339. Two variant full-length cDNA sequences for P510S are provided in SEQ ID NO: 535 and 536, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 537 and 538, respectively. Additional splice variants of P510S are provided in SEQ ID NO: 598 and 599.

The determined cDNA sequences for additional prostate-specific clones isolated during characterization of prostate specific cDNA libraries are provided in SEQ ID NO: 618-689, 691-697 and 709-772. Comparison of these sequences with those in the public databases revealed no significant homologies to any of these sequences.

## EXAMPLE 2

## DETERMINATION OF TISSUE SPECIFICITY OF PROSTATE-SPECIFIC POLYPEPTIDES

5           Using gene specific primers, mRNA expression levels for the representative prostate-specific polypeptides F1-16, H1-1, J1-17 (also referred to as P502S), L1-12 (also referred to as P501S), F1-12 (also referred to as P504S) and N1-1862 (also referred to as P503S) were examined in a variety of normal and tumor tissues using RT-PCR.

10           Briefly, total RNA was extracted from a variety of normal and tumor tissues using Trizol reagent as described above. First strand synthesis was carried out using 1-2  $\mu$ g of total RNA with SuperScript II reverse transcriptase (BRL Life Technologies) at 42 °C for one hour. The cDNA was then amplified by PCR with gene-specific primers. To ensure the semi-quantitative nature of the RT-PCR,  $\beta$ -actin was  
15           used as an internal control for each of the tissues examined. First, serial dilutions of the first strand cDNAs were prepared and RT-PCR assays were performed using  $\beta$ -actin specific primers. A dilution was then chosen that enabled the linear range amplification of the  $\beta$ -actin template and which was sensitive enough to reflect the differences in the initial copy numbers. Using these conditions, the  $\beta$ -actin levels were determined for  
20           each reverse transcription reaction from each tissue. DNA contamination was minimized by DNase treatment and by assuring a negative PCR result when using first strand cDNA that was prepared without adding reverse transcriptase.

          mRNA Expression levels were examined in four different types of tumor tissue (prostate tumor from 2 patients, breast tumor from 3 patients, colon tumor, lung  
25           tumor), and sixteen different normal tissues, including prostate, colon, kidney, liver, lung, ovary, pancreas, skeletal muscle, skin, stomach, testes, bone marrow and brain. F1-16 was found to be expressed at high levels in prostate tumor tissue, colon tumor and normal prostate, and at lower levels in normal liver, skin and testes, with expression being undetectable in the other tissues examined. H1-1 was found to be expressed at  
30           high levels in prostate tumor, lung tumor, breast tumor, normal prostate, normal colon



and normal brain, at much lower levels in normal lung, pancreas, skeletal muscle, skin, small intestine, bone marrow, and was not detected in the other tissues tested. J1-17 (P502S) and L1-12 (P501S) appear to be specifically over-expressed in prostate, with both genes being expressed at high levels in prostate tumor and normal prostate but at low to undetectable levels in all the other tissues examined. N1-1862 (P503S) was found to be over-expressed in 60% of prostate tumors and detectable in normal colon and kidney. The RT-PCR results thus indicate that F1-16, H1-1, J1-17 (P502S), N1-1862 (P503S) and L1-12 (P501S) are either prostate specific or are expressed at significantly elevated levels in prostate.

Further RT-PCR studies showed that F1-12 (P504S) is over-expressed in 60% of prostate tumors, detectable in normal kidney but not detectable in all other tissues tested. Similarly, R1-2330 was shown to be over-expressed in 40% of prostate tumors, detectable in normal kidney and liver, but not detectable in all other tissues tested. U1-3064 was found to be over-expressed in 60% of prostate tumors, and also expressed in breast and colon tumors, but was not detectable in normal tissues.

RT-PCR characterization of R1-2330, U1-3064 and 1D-4279 showed that these three antigens are over-expressed in prostate and/or prostate tumors.

Northern analysis with four prostate tumors, two normal prostate samples, two BPH prostates, and normal colon, kidney, liver, lung, pancreas, skeletal muscle, brain, stomach, testes, small intestine and bone marrow, showed that L1-12 (P501S) is over-expressed in prostate tumors and normal prostate, while being undetectable in other normal tissues tested. J1-17 (P502S) was detected in two prostate tumors and not in the other tissues tested. N1-1862 (P503S) was found to be over-expressed in three prostate tumors and to be expressed in normal prostate, colon and kidney, but not in other tissues tested. F1-12 (P504S) was found to be highly expressed in two prostate tumors and to be undetectable in all other tissues tested.

The microarray technology described above was used to determine the expression levels of representative antigens described herein in prostate tumor, breast tumor and the following normal tissues: prostate, liver, pancreas, skin, bone marrow, brain, breast, adrenal gland, bladder, testes, salivary gland, large intestine, kidney,

ovary, lung, spinal cord, skeletal muscle and colon. L1-12 (P501S) was found to be over-expressed in normal prostate and prostate tumor, with some expression being detected in normal skeletal muscle. Both J1-12 and F1-12 (P504S) were found to be over-expressed in prostate tumor, with expression being lower or undetectable in all other tissues tested. N1-1862 (P503S) was found to be expressed at high levels in prostate tumor and normal prostate, and at low levels in normal large intestine and normal colon, with expression being undetectable in all other tissues tested. R1-2330 was found to be over-expressed in prostate tumor and normal prostate, and to be expressed at lower levels in all other tissues tested. 1D-4279 was found to be over-expressed in prostate tumor and normal prostate, expressed at lower levels in normal spinal cord, and to be undetectable in all other tissues tested.

Further microarray analysis to specifically address the extent to which P501S (SEQ ID NO: 110) was expressed in breast tumor revealed moderate over-expression not only in breast tumor, but also in metastatic breast tumor (2/31), with negligible to low expression in normal tissues. This data suggests that P501S may be over-expressed in various breast tumors as well as in prostate tumors.

The expression levels of 32 ESTs (expressed sequence tags) described by Vasmatzis *et al.* (*Proc. Natl. Acad. Sci. USA* 95:300-304, 1998) in a variety of tumor and normal tissues were examined by microarray technology as described above. Two of these clones (referred to as P1000C and P1001C) were found to be over-expressed in prostate tumor and normal prostate, and expressed at low to undetectable levels in all other tissues tested (normal aorta, thymus, resting and activated PBMC, epithelial cells, spinal cord, adrenal gland, fetal tissues, skin, salivary gland, large intestine, bone marrow, liver, lung, dendritic cells, stomach, lymph nodes, brain, heart, small intestine, skeletal muscle, colon and kidney. The determined cDNA sequences for P1000C and P1001C are provided in SEQ ID NO: 384 and 472, respectively. The sequence of P1001C was found to show some homology to the previously isolated Human mRNA for JM27 protein. Subsequent comparison of the sequence of SEQ ID NO: 384 with sequences in the public databases, led to the identification of a full-length cDNA sequence of P1000C (SEQ ID NO: 929), which encodes a 492 amino acid sequence.

Analysis of the amino acid sequence using the PSORT II program led to the identification of a putative transmembrane domain from amino acids 84-100. The cDNA sequence of the open reading frame of P1000C, including the stop codon, is provided in SEQ ID NO: 930, with the open reading frame without the stop codon being  
5 provided in SEQ ID NO: 931. The full-length amino acid sequence of P1000C is provided in SEQ ID NO: 932. SEQ ID NO: 933 and 934 represent amino acids 1-100 and 100-492 of P1000C, respectively.

The expression of the polypeptide encoded by the full length cDNA sequence for F1-12 (also referred to as P504S; SEQ ID NO: 108) was investigated by  
10 immunohistochemical analysis. Rabbit-anti-P504S polyclonal antibodies were generated against the full length P504S protein by standard techniques. Subsequent isolation and characterization of the polyclonal antibodies were also performed by techniques well known in the art. Immunohistochemical analysis showed that the P504S polypeptide was expressed in 100% of prostate carcinoma samples tested (n=5).

15 The rabbit-anti-P504S polyclonal antibody did not appear to label benign prostate cells with the same cytoplasmic granular staining, but rather with light nuclear staining. Analysis of normal tissues revealed that the encoded polypeptide was found to be expressed in some, but not all normal human tissues. Positive cytoplasmic staining with rabbit-anti-P504S polyclonal antibody was found in normal human kidney, liver,  
20 brain, colon and lung-associated macrophages, whereas heart and bone marrow were negative.

This data indicates that the P504S polypeptide is present in prostate cancer tissues, and that there are qualitative and quantitative differences in the staining between benign prostatic hyperplasia tissues and prostate cancer tissues, suggesting that  
25 this polypeptide may be detected selectively in prostate tumors and therefore be useful in the diagnosis of prostate cancer.

## EXAMPLE 3

ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC  
POLYPEPTIDES BY PCR-BASED SUBTRACTION

5 A cDNA subtraction library, containing cDNA from normal prostate subtracted with ten other normal tissue cDNAs (brain, heart, kidney, liver, lung, ovary, placenta, skeletal muscle, spleen and thymus) and then submitted to a first round of PCR amplification, was purchased from Clontech. This library was subjected to a second round of PCR amplification, following the manufacturer's protocol. The  
10 resulting cDNA fragments were subcloned into the vector pT7 Blue T-vector (Novagen, Madison, WI) and transformed into XL-1 Blue MRF' *E. coli* (Stratagene). DNA was isolated from independent clones and sequenced using a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A.

Fifty-nine positive clones were sequenced. Comparison of the DNA  
15 sequences of these clones with those in the gene bank, as described above, revealed no significant homologies to 25 of these clones, hereinafter referred to as P5, P8, P9, P18, P20, P30, P34, P36, P38, P39, P42, P49, P50, P53, P55, P60, P64, P65, P73, P75, P76, P79 and P84. The determined cDNA sequences for these clones are provided in SEQ ID NO: 41-45, 47-52 and 54-65, respectively. P29, P47, P68, P80 and P82 (SEQ ID  
20 NO: 46, 53 and 66-68, respectively) were found to show some degree of homology to previously identified DNA sequences. To the best of the inventors' knowledge, none of these sequences have been previously shown to be present in prostate.

Further studies employing the sequence of SEQ ID NO: 67 as a probe in standard full-length cloning methods, resulted in the isolation of three cDNA sequences  
25 which appear to be splice variants of P80 (also known as P704P). These sequences are provided in SEQ ID NO: 699-701.

Further studies using the PCR-based methodology described above resulted in the isolation of more than 180 additional clones, of which 23 clones were found to show no significant homologies to known sequences. The determined cDNA  
30 sequences for these clones are provided in SEQ ID NO: 115-123, 127, 131, 137, 145,

147-151, 153, 156-158 and 160. Twenty-three clones (SEQ ID NO: 124-126, 128-130, 132-136, 138-144, 146, 152, 154, 155 and 159) were found to show some homology to previously identified ESTs. An additional ten clones (SEQ ID NO: 161-170) were found to have some degree of homology to known genes. Larger cDNA clones  
5 containing the P20 sequence represent splice variants of a gene referred to as P703P. The determined DNA sequence for the variants referred to as DE1, DE13 and DE14 are provided in SEQ ID NOS: 171, 175 and 177, respectively, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 172, 176 and 178, respectively. The determined cDNA sequence for an extended spliced form of P703 is  
10 provided in SEQ ID NO: 225. The DNA sequences for the splice variants referred to as DE2 and DE6 are provided in SEQ ID NOS: 173 and 174, respectively.

mRNA Expression levels for representative clones in tumor tissues (prostate (n=5), breast (n=2), colon and lung) normal tissues (prostate (n=5), colon, kidney, liver, lung (n=2), ovary (n=2), skeletal muscle, skin, stomach, small intestine  
15 and brain), and activated and non-activated PBMC was determined by RT-PCR as described above. Expression was examined in one sample of each tissue type unless otherwise indicated.

P9 was found to be highly expressed in normal prostate and prostate tumor compared to all normal tissues tested except for normal colon which showed  
20 comparable expression. P20, a portion of the P703P gene, was found to be highly expressed in normal prostate and prostate tumor, compared to all twelve normal tissues tested. A modest increase in expression of P20 in breast tumor (n=2), colon tumor and lung tumor was seen compared to all normal tissues except lung (1 of 2). Increased expression of P18 was found in normal prostate, prostate tumor and breast tumor  
25 compared to other normal tissues except lung and stomach. A modest increase in expression of P5 was observed in normal prostate compared to most other normal tissues. However, some elevated expression was seen in normal lung and PBMC. Elevated expression of P5 was also observed in prostate tumors (2 of 5), breast tumor and one lung tumor sample. For P30, similar expression levels were seen in normal  
30 prostate and prostate tumor, compared to six of twelve other normal tissues tested.

Increased expression was seen in breast tumors, one lung tumor sample and one colon tumor sample, and also in normal PBMC. P29 was found to be over-expressed in prostate tumor (5 of 5) and normal prostate (5 of 5) compared to the majority of normal tissues. However, substantial expression of P29 was observed in normal colon and  
5 normal lung (2 of 2). P80 was found to be over-expressed in prostate tumor (5 of 5) and normal prostate (5 of 5) compared to all other normal tissues tested, with increased expression also being seen in colon tumor.

Further studies resulted in the isolation of twelve additional clones, hereinafter referred to as 10-d8, 10-h10, 11-c8, 7-g6, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3, 8-  
10 h11, 9-f12 and 9-f3. The determined DNA sequences for 10-d8, 10-h10, 11-c8, 8-d4, 8-d9, 8-h11, 9-f12 and 9-f3 are provided in SEQ ID NO: 207, 208, 209, 216, 217, 220, 221 and 222, respectively. The determined forward and reverse DNA sequences for 7-g6, 8-b5, 8-b6 and 8-g3 are provided in SEQ ID NO: 210 and 211; 212 and 213; 214 and 215; and 218 and 219, respectively. Comparison of these sequences with those in  
15 the gene bank revealed no significant homologies to the sequence of 9-f3. The clones 10-d8, 11-c8 and 8-h11 were found to show some homology to previously isolated ESTs, while 10-h10, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3 and 9-f12 were found to show some homology to previously identified genes. Further characterization of 7-G6 and 8-G3 showed identity to the known genes PAP and PSA, respectively.

20 mRNA expression levels for these clones were determined using the micro-array technology described above. The clones 7-G6, 8-G3, 8-B5, 8-B6, 8-D4, 8-D9, 9-F3, 9-F12, 9-H3, 10-A2, 10-A4, 11-C9 and 11-F2 were found to be over-expressed in prostate tumor and normal prostate, with expression in other tissues tested being low or undetectable. Increased expression of 8-F11 was seen in prostate tumor  
25 and normal prostate, bladder, skeletal muscle and colon. Increased expression of 10-H10 was seen in prostate tumor and normal prostate, bladder, lung, colon, brain and large intestine. Increased expression of 9-B1 was seen in prostate tumor, breast tumor, and normal prostate, salivary gland, large intestine and skin, with increased expression of 11-C8 being seen in prostate tumor, and normal prostate and large intestine.

An additional cDNA fragment derived from the PCR-based normal prostate subtraction, described above, was found to be prostate specific by both microarray technology and RT-PCR. The determined cDNA sequence of this clone (referred to as 9-A11) is provided in SEQ ID NO: 226. Comparison of this sequence with those  
5 in the public databases revealed 99% identity to the known gene HOXB13.

Further studies led to the isolation of the clones 8-C6 and 8-H7. The determined cDNA sequences for these clones are provided in SEQ ID NO: 227 and 228, respectively. These sequences were found to show some homology to previously isolated ESTs.

10 PCR and hybridization-based methodologies were employed to obtain longer cDNA sequences for clone P20 (also referred to as P703P), yielding three additional cDNA fragments that progressively extend the 5' end of the gene. These fragments, referred to as P703PDE5, P703P6.26, and P703PX-23 (SEQ ID NO: 326, 328 and 330, with the predicted corresponding amino acid sequences being provided in  
15 SEQ ID NO: 327, 329 and 331, respectively) contain additional 5' sequence. P703PDE5 was recovered by screening of a cDNA library (#141-26) with a portion of P703P as a probe. P703P6.26 was recovered from a mixture of three prostate tumor cDNAs and P703PX\_23 was recovered from cDNA library (#438-48). Together, the additional sequences include all of the putative mature serine protease along with part of  
20 the putative signal sequence. The full-length cDNA sequence for P703P is provided in SEQ ID NO: 524, with the corresponding amino acid sequence being provided in SEQ ID NO: 525.

Using computer algorithms, the following regions of P703P were predicted to represent potential HLA A2-binding CTL epitopes: amino acids 164-172  
25 of SEQ ID NO: 525 (SEQ ID NO: 866); amino acids 160-168 of SEQ ID NO: 525 (SEQ ID NO: 867); amino acids 239-247 of SEQ ID NO: 525 (SEQ ID NO: 868); amino acids 118-126 of SEQ ID NO: 525 (SEQ ID NO: 869); amino acids 112-120 of SEQ ID NO: 525 (SEQ ID NO: 870); amino acids 155-164 of SEQ ID NO: 525 (SEQ ID NO: 871); amino acids 117-126 of SEQ ID NO: 525 (SEQ ID NO: 872); amino acids  
30 164-173 of SEQ ID NO: 525 (SEQ ID NO: 873); amino acids 154-163 of SEQ ID NO:

525 (SEQ ID NO: 874); amino acids 163-172 of SEQ ID NO: 525 (SEQ ID NO: 875); amino acids 58-66 of SEQ ID NO: 525 (SEQ ID NO: 876); and amino acids 59-67 of SEQ ID NO: 525 (SEQ ID NO: 877).

P703P was found to show some homology to previously identified proteases, such as thrombin. The thrombin receptor has been shown to be preferentially expressed in highly metastatic breast carcinoma cells and breast carcinoma biopsy samples. Introduction of thrombin receptor antisense cDNA has been shown to inhibit the invasion of metastatic breast carcinoma cells in culture. Antibodies against thrombin receptor inhibit thrombin receptor activation and thrombin-induced platelet activation. Furthermore, peptides that resemble the receptor's tethered ligand domain inhibit platelet aggregation by thrombin. P703P may play a role in prostate cancer through a protease-activated receptor on the cancer cell or on stromal cells. The potential trypsin-like protease activity of P703P may either activate a protease-activated receptor on the cancer cell membrane to promote tumorigenesis or activate a protease-activated receptor on the adjacent cells (such as stromal cells) to secrete growth factors and/or proteases (such as matrix metalloproteinases) that could promote tumor angiogenesis, invasion and metastasis. P703P may thus promote tumor progression and/or metastasis through the activation of protease-activated receptor. Polypeptides and antibodies that block the P703P-receptor interaction may therefore be usefully employed in the treatment of prostate cancer.

To determine whether P703P expression increases with increased severity of Gleason grade, an indicator of tumor stage, quantitative PCR analysis was performed on prostate tumor samples with a range of Gleason scores from 5 to > 8. The mean level of P703P expression increased with increasing Gleason score, indicating that P703P expression may correlate with increased disease severity.

Further studies using a PCR-based subtraction library of a prostate tumor pool subtracted against a pool of normal tissues (referred to as JP: PCR subtraction) resulted in the isolation of thirteen additional clones, seven of which did not share any significant homology to known GenBank sequences. The determined cDNA sequences for these seven clones (P711P, P712P, novel 23, P774P, P775P, P710P and P768P) are



provided in SEQ ID NO: 307-311, 313 and 315, respectively. The remaining six clones (SEQ ID NO: 316 and 321-325) were shown to share some homology to known genes. By microarray analysis, all thirteen clones showed three or more fold over-expression in prostate tissues, including prostate tumors, BPH and normal prostate as compared to normal non-prostate tissues. Clones P711P, P712P, novel 23 and P768P showed over-expression in most prostate tumors and BPH tissues tested (n=29), and in the majority of normal prostate tissues (n=4), but background to low expression levels in all normal tissues. Clones P774P, P775P and P710P showed comparatively lower expression and expression in fewer prostate tumors and BPH samples, with negative to low expression in normal prostate.

Further studies led to the isolation of an extended cDNA sequence for P712P (SEQ ID NO: 552). The amino acid sequences encoded by 16 predicted open reading frames present within the sequence of SEQ ID NO: 552 are provided in SEQ ID NO: 553-568.

The full-length cDNA for P711P was obtained by employing the partial sequence of SEQ ID NO: 307 to screen a prostate cDNA library. Specifically, a directionally cloned prostate cDNA library was prepared using standard techniques. One million colonies of this library were plated onto LB/Amp plates. Nylon membrane filters were used to lift these colonies, and the cDNAs which were picked up by these filters were denatured and cross-linked to the filters by UV light. The P711P cDNA fragment of SEQ ID NO: 307 was radio-labeled and used to hybridize with these filters. Positive clones were selected, and cDNAs were prepared and sequenced using an automatic Perkin Elmer/Applied Biosystems sequencer. The determined full-length sequence of P711P is provided in SEQ ID NO: 382, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 383.

Using PCR and hybridization-based methodologies, additional cDNA sequence information was derived for two clones described above, 11-C9 and 9-F3, herein after referred to as P707P and P714P, respectively (SEQ ID NO: 333 and 334). After comparison with the most recent GenBank, P707P was found to be a splice variant of the known gene HoxB13. In contrast, no significant homologies to P714P

were found. Further studies employing the sequence of SEQ ID NO: 334 as a probe in standard full-length cloning methods, resulted in an extended cDNA sequence for P714P. This sequence is provided in SEQ ID NO: 698. This sequence was found to show some homology to the gene that encodes human ribosomal L23A protein.

5 Clones 8-B3, P89, P98, P130 and P201 (as disclosed in U.S. Patent Application No. 09/020,956, filed February 9, 1998) were found to be contained within one contiguous sequence, referred to as P705P (SEQ ID NO: 335, with the predicted amino acid sequence provided in SEQ ID NO: 336), which was determined to be a splice variant of the known gene NKX 3.1.

10 Further studies on P775P resulted in the isolation of four additional sequences (SEQ ID NO: 473-476) which are all splice variants of the P775P gene. The sequence of SEQ ID NO: 474 was found to contain two open reading frames (ORFs). The predicted amino acid sequences encoded by these ORFs are provided in SEQ ID NO: 477 and 478. The cDNA sequence of SEQ ID NO: 475 was found to contain an  
15 ORF which encodes the amino acid sequence of SEQ ID NO: 479. The cDNA sequence of SEQ ID NO: 473 was found to contain four ORFs. The predicted amino acid sequences encoded by these ORFs are provided in SEQ ID NO: 480-483. Additional splice variants of P775P are provided in SEQ ID NO: 593-597.

Subsequent studies led to the identification of a genomic region on  
20 chromosome 22q11.2, known as the Cat Eye Syndrome region, that contains the five prostate genes P704P, P712P, P774P, P775P and B305D. The relative location of each of these five genes within the genomic region is shown in Fig. 10. This region may therefore be associated with malignant tumors, and other potential tumor genes may be contained within this region. These studies also led to the identification of a potential  
25 open reading frame (ORF) for P775P (provided in SEQ ID NO: 533), which encodes the amino acid sequence of SEQ ID NO: 534.

Comparison of the clone of SEQ ID NO: 325 (referred to as P558S) with sequences in the GenBank and GeneSeq DNA databases showed that P558S is identical to the prostate-specific transglutaminase gene, which is known to have two forms. The  
30 full-length sequences for the two forms are provided in SEQ ID NO: 773 and 774, with

the corresponding amino acid sequences being provided in SEQ ID NO: 775 and 776, respectively. The cDNA sequence of SEQ ID NO: 774 has a 15 pair base insert, resulting in a 5 amino acid insert in the corresponding amino acid sequence (SEQ ID NO: 776). This insert is not present in the sequence of SEQ ID NO: 773.

5 Further studies on P768P (SEQ ID NO: 315) led to the identification of the putative full-length open reading frame (ORF). The cDNA sequence of the ORF with stop codon is provided in SEQ ID NO: 907. The cDNA sequence of the ORF without stop codon is provided in SEQ ID NO: 908, with the corresponding amino acid sequence being provided in SEQ ID NO: 909. This sequence was found to show 86%  
10 identity to a rat calcium transporter protein, indicating that P768P may represent a human calcium transporter protein. The locations of transmembrane domains within P768P were predicted using the PSORT II computer algorithm. Six transmembrane domains were predicted at amino acid positions 118-134, 172-188, 211-227, 230-246, 282-298 and 348-364. The amino acid sequences of SEQ ID NO: 910-915 represent  
15 amino acids 1-134, 135-188, 189-227, 228-246, 247-298 and 299-511 of P768P, respectively.

#### EXAMPLE 4

##### SYNTHESIS OF POLYPEPTIDES

20

Polypeptides may be synthesized on a Perkin Elmer/Applied Biosystems 430A peptide synthesizer using Fmoc chemistry with HPTU (O-Benzotriazole-N,N,N',N'-tetramethyluronium hexafluorophosphate) activation. A Gly-Cys-Gly sequence may be attached to the amino terminus of the peptide to provide a method of  
25 conjugation, binding to an immobilized surface, or labeling of the peptide. Cleavage of the peptides from the solid support may be carried out using the following cleavage mixture: trifluoroacetic acid:ethanedithiol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for 2 hours, the peptides may be precipitated in cold methyl-t-butyl-ether. The peptide pellets may then be dissolved in water containing 0.1% trifluoroacetic acid  
30 (TFA) and lyophilized prior to purification by C18 reverse phase HPLC. A gradient of

0%-60% acetonitrile (containing 0.1% TFA) in water (containing 0.1% TFA) may be used to elute the peptides. Following lyophilization of the pure fractions, the peptides may be characterized using electrospray or other types of mass spectrometry and by amino acid analysis.

5

## EXAMPLE 5

### FURTHER ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC POLYPEPTIDES BY PCR-BASED SUBTRACTION

10 A cDNA library generated from prostate primary tumor mRNA as described above was subtracted with cDNA from normal prostate. The subtraction was performed using a PCR-based protocol (Clontech), which was modified to generate larger fragments. Within this protocol, tester and driver double stranded cDNA were separately digested with five restriction enzymes that recognize six-nucleotide  
15 restriction sites (MluI, MscI, PvuII, SalI and StuI). This digestion resulted in an average cDNA size of 600 bp, rather than the average size of 300 bp that results from digestion with RsaI according to the Clontech protocol. This modification did not affect the subtraction efficiency. Two tester populations were then created with different adapters, and the driver library remained without adapters.

20 The tester and driver libraries were then hybridized using excess driver cDNA. In the first hybridization step, driver was separately hybridized with each of the two tester cDNA populations. This resulted in populations of (a) unhybridized tester cDNAs, (b) tester cDNAs hybridized to other tester cDNAs, (c) tester cDNAs hybridized to driver cDNAs and (d) unhybridized driver cDNAs. The two separate  
25 hybridization reactions were then combined, and rehybridized in the presence of additional denatured driver cDNA. Following this second hybridization, in addition to populations (a) through (d), a fifth population (e) was generated in which tester cDNA with one adapter hybridized to tester cDNA with the second adapter. Accordingly, the second hybridization step resulted in enrichment of differentially expressed sequences  
30 which could be used as templates for PCR amplification with adaptor-specific primers.

The ends were then filled in, and PCR amplification was performed using adaptor-specific primers. Only population (e), which contained tester cDNA that did not hybridize to driver cDNA, was amplified exponentially. A second PCR amplification step was then performed, to reduce background and further enrich  
5 differentially expressed sequences.

This PCR-based subtraction technique normalizes differentially expressed cDNAs so that rare transcripts that are overexpressed in prostate tumor tissue may be recoverable. Such transcripts would be difficult to recover by traditional subtraction methods.

10 In addition to genes known to be overexpressed in prostate tumor, seventy-seven further clones were identified. Sequences of these partial cDNAs are provided in SEQ ID NO: 29 to 305. Most of these clones had no significant homology to database sequences. Exceptions were JPTPN23 (SEQ ID NO: 231; similarity to pig valosin-containing protein), JPTPN30 (SEQ ID NO: 234; similarity to rat mRNA for  
15 proteasome subunit), JPTPN45 (SEQ ID NO: 243; similarity to rat *norvegicus* cytosolic NADP-dependent isocitrate dehydrogenase), JPTPN46 (SEQ ID NO: 244; similarity to human subclone H8 4 d4 DNA sequence), JP1D6 (SEQ ID NO: 265; similarity to *G. gallus* dynein light chain-A), JP8D6 (SEQ ID NO: 288; similarity to human BAC clone RG016J04), JP8F5 (SEQ ID NO: 289; similarity to human subclone H8 3 b5 DNA  
20 sequence), and JP8E9 (SEQ ID NO: 299; similarity to human Alu sequence).

Additional studies using the PCR-based subtraction library consisting of a prostate tumor pool subtracted against a normal prostate pool (referred to as PT-PN PCR subtraction) yielded three additional clones. Comparison of the cDNA sequences of these clones with the most recent release of GenBank revealed no significant  
25 homologies to the two clones referred to as P715P and P767P (SEQ ID NO: 312 and 314). The remaining clone was found to show some homology to the known gene KIAA0056 (SEQ ID NO: 318). Using microarray analysis to measure mRNA expression levels in various tissues, all three clones were found to be over-expressed in prostate tumors and BPH tissues. Specifically, clone P715P was over-expressed in most  
30 prostate tumors and BPH tissues by a factor of three or greater, with elevated expression

seen in the majority of normal prostate samples and in fetal tissue, but negative to low expression in all other normal tissues. Clone P767P was over-expressed in several prostate tumors and BPH tissues, with moderate expression levels in half of the normal prostate samples, and background to low expression in all other normal tissues tested.

5 Further analysis, by microarray as described above, of the PT-PN PCR subtraction library and of a DNA subtraction library containing cDNA from prostate tumor subtracted with a pool of normal tissue cDNAs, led to the isolation of 27 additional clones (SEQ ID NO: 340-365 and 381) which were determined to be over-expressed in prostate tumor. The clones of SEQ ID NO: 341, 342, 345, 347, 348, 349,  
10 351, 355-359, 361, 362 and 364 were also found to be expressed in normal prostate. Expression of all 26 clones in a variety of normal tissues was found to be low or undetectable, with the exception of P544S (SEQ ID NO: 356) which was found to be expressed in small intestine. Of the 26 clones, 11 (SEQ ID NO: 340-349 and 362) were found to show some homology to previously identified sequences. No significant  
15 homologies were found to the clones of SEQ ID NO: 350, 351, 353-361, and 363-365.

Comparison of the sequence of SEQ ID NO: 362 with sequences in the GenBank and GeneSeq DNA databases showed that this clone (referred to as P788P) is identical to GeneSeq Accession No. X27262, which encodes a protein found in the GeneSeq protein Accession No. Y00931. The full length cDNA sequence of P788P is  
20 shown in Figure 12A (SEQ ID NO: 777), with the corresponding predicted amino acid being shown in Figure 12B (SEQ ID NO: 778). Subsequently, a full-length cDNA sequence for P788P that contains polymorphisms not found in the sequence of SEQ ID NO: 779, was cloned multiple times by PCR amplification from cDNA prepared from several RNA templates from three individuals. This determined cDNA sequence of this  
25 polymorphic variant of P788P is provided in SEQ ID NO: 779, with the corresponding amino acid sequence being provided in SEQ ID NO: 780. The sequence of SEQ ID NO: 780 differs from that of SEQ ID NO: 778 by six amino acid residues. The P788P protein has 7 potential transmembrane domains at the C-terminal portion and is predicted to be a plasma membrane protein with an extracellular N-terminal region.

Further studies on the clone of SEQ ID NO: 352 (referred to as P790P) led to the isolation of the full-length cDNA sequence of SEQ ID NO: 526. The corresponding predicted amino acid is provided in SEQ ID NO: 527. Data from two quantitative PCR experiments indicated that P790P is over-expressed in 11/15 tested prostate tumor samples and is expressed at low levels in spinal cord, with no expression being seen in all other normal samples tested. Data from further PCR experiments and microarray experiments showed over-expression in normal prostate and prostate tumor with little or no expression in other tissues tested. P790P was subsequently found to show significant homology to a previously identified G-protein coupled prostate tissue receptor.

Additional studies on the clone of SEQ ID NO: 354 (referred to as P776P) led to the isolation of an extended cDNA sequence, provided in SEQ ID NO: 569. The determined cDNA sequences of three additional splice variants of P776P are provided in SEQ ID NO: 570-572. The amino acid sequences encoded by two predicted open reading frames (ORFs) contained within SEQ ID NO: 570, one predicted ORF contained within SEQ ID NO: 571, and 11 predicted ORFs contained within SEQ ID NO: 569, are provided in SEQ ID NO: 573-586, respectively. Further studies led to the isolation of the full-length sequence for the clone of SEQ ID NO: 570 (provided in SEQ ID NO: 880). Full-length cloning efforts on the clone of SEQ ID NO: 571 led to the isolation of two sequences (provided in SEQ ID NO: 881 and 882), representing a single clone, that are identical with the exception of a polymorphic insertion/deletion at position 1293. Specifically, the clone of SEQ ID NO: 882 (referred to as clone F1) has a C at position 1293. The clone of SEQ ID NO: 881 (referred to as clone F2) has a single base pair deletion at position 1293. The predicted amino acid sequences encoded by 5 open reading frames located within SEQ ID NO: 880 are provided in SEQ ID NO: 883-887, with the predicted amino acid sequences encoded by the clone of SEQ ID NO: 881 and 882 being provided in SEQ ID NO: 888-893.

Comparison of the cDNA sequences for the clones P767P (SEQ ID NO: 314) and P777P (SEQ ID NO: 350) with sequences in the GenBank human EST database showed that the two clones matched many EST sequences in common,

suggesting that P767P and P777P may represent the same gene. A DNA consensus sequence derived from a DNA sequence alignment of P767P, P777P and multiple EST clones is provided in SEQ ID NO: 587. The amino acid sequences encoded by three putative ORFs located within SEQ ID NO: 587 are provided in SEQ ID NO: 588-590.

- 5           The clone of SEQ ID NO: 342 (referred to as P789P) was found to show homology to a previously identified gene. The full length cDNA sequence for P789P and the corresponding amino acid sequence are provided in SEQ ID NO: 878 and 879, respectively.

10

## EXAMPLE 6

### PEPTIDE PRIMING OF MICE AND PROPAGATION OF CTL LINES

6.1. This Example illustrates the preparation of a CTL cell line specific for cells expressing the P502S gene.

- 15           Mice expressing the transgene for human HLA A2Kb (provided by Dr L. Sherman, The Scripps Research Institute, La Jolla, CA) were immunized with P2S#12 peptide (VLGWVAEL; SEQ ID NO: 306), which is derived from the P502S gene (also referred to herein as J1-17, SEQ ID NO: 8), as described by Theobald et al., *Proc. Natl. Acad. Sci. USA* 92:11993-11997, 1995 with the following modifications. Mice were
- 20 immunized with 100 $\mu$ g of P2S#12 and 120 $\mu$ g of an I-A<sup>b</sup> binding peptide derived from hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and using a nylon mesh single cell suspensions prepared. Cells were then resuspended at  $6 \times 10^6$  cells/ml in complete media (RPMI-1640; Gibco BRL, Gaithersburg, MD) containing 10% FCS, 2mM Glutamine (Gibco BRL), sodium
- 25 pyruvate (Gibco BRL), non-essential amino acids (Gibco BRL),  $2 \times 10^{-5}$  M 2-mercaptoethanol, 50U/ml penicillin and streptomycin, and cultured in the presence of irradiated (3000 rads) P2S#12-pulsed (5mg/ml P2S#12 and 10mg/ml  $\beta$ 2-microglobulin) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7 $\mu$ g/ml dextran sulfate and 25 $\mu$ g/ml LPS for 3 days). Six days later, cells ( $5 \times 10^5$ /ml) were
- 30 restimulated with  $2.5 \times 10^6$ /ml peptide pulsed irradiated (20,000 rads) EL4A2Kb cells



(Sherman et al, *Science* 258:815-818, 1992) and  $3 \times 10^6$ /ml A2 transgenic spleen feeder cells. Cells were cultured in the presence of 20U/ml IL-2. Cells continued to be restimulated on a weekly basis as described, in preparation for cloning the line.

P2S#12 line was cloned by limiting dilution analysis with peptide pulsed  
5 EL4 A2Kb tumor cells ( $1 \times 10^4$  cells/ well) as stimulators and A2 transgenic spleen cells as feeders ( $5 \times 10^5$  cells/ well) grown in the presence of 30U/ml IL-2. On day 14, cells were restimulated as before. On day 21, clones that were growing were isolated and maintained in culture. Several of these clones demonstrated significantly higher reactivity (lysis) against human fibroblasts (HLA A2Kb expressing) transduced with  
10 P502S than against control fibroblasts. An example is presented in Figure 1.

This data indicates that P2S #12 represents a naturally processed epitope of the P502S protein that is expressed in the context of the human HLA A2Kb molecule.

15 6.2. This Example illustrates the preparation of murine CTL lines and CTL clones specific for cells expressing the P501S gene.

This series of experiments were performed similarly to that described above. Mice were immunized with the P1S#10 peptide (SEQ ID NO: 337), which is  
20 derived from the P501S gene (also referred to herein as L1-12, SEQ ID NO: 110). The P1S#10 peptide was derived by analysis of the predicted polypeptide sequence for P501S for potential HLA-A2 binding sequences as defined by published HLA-A2 binding motifs (Parker, KC, et al, *J. Immunol.*, 152:163, 1994). P1S#10 peptide was synthesized as described in Example 4, and empirically tested for HLA-A2 binding  
25 using a T cell based competition assay. Predicted A2 binding peptides were tested for their ability to compete HLA-A2 specific peptide presentation to an HLA-A2 restricted CTL clone (D150M58), which is specific for the HLA-A2 binding influenza matrix peptide fluM58. D150M58 CTL secretes TNF in response to self-presentation of peptide fluM58. In the competition assay, test peptides at 100-200  $\mu$ g/ml were added to  
30 cultures of D150M58 CTL in order to bind HLA-A2 on the CTL. After thirty minutes,

CTL cultured with test peptides, or control peptides, were tested for their antigen dose response to the fluM58 peptide in a standard TNF bioassay. As shown in Figure 3, peptide P1S#10 competes HLA-A2 restricted presentation of fluM58, demonstrating that peptide P1S#10 binds HLA-A2.

5 Mice expressing the transgene for human HLA A2Kb were immunized as described by Theobald et al. (*Proc. Natl. Acad. Sci. USA* 92:11993-11997, 1995) with the following modifications. Mice were immunized with 62.5 $\mu$ g of P1S #10 and 120 $\mu$ g of an I-A<sup>b</sup> binding peptide derived from Hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and single  
10 cell suspensions prepared using a nylon mesh. Cells were then resuspended at  $6 \times 10^6$  cells/ml in complete media (as described above) and cultured in the presence of irradiated (3000 rads) P1S#10-pulsed (2 $\mu$ g/ml P1S#10 and 10mg/ml  $\beta$ 2-microglobulin) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7 $\mu$ g/ml dextran sulfate and 25 $\mu$ g/ml LPS for 3 days). Six days later cells ( $5 \times 10^5$ /ml) were restimulated  
15 with  $2.5 \times 10^6$ /ml peptide-pulsed irradiated (20,000 rads) EL4A2Kb cells, as described above, and  $3 \times 10^6$ /ml A2 transgenic spleen feeder cells. Cells were cultured in the presence of 20 U/ml IL-2. Cells were restimulated on a weekly basis in preparation for cloning. After three rounds of *in vitro* stimulations, one line was generated that recognized P1S#10-pulsed Jurkat A2Kb targets and P501S-transduced Jurkat targets as  
20 shown in Figure 4.

A P1S#10-specific CTL line was cloned by limiting dilution analysis with peptide pulsed EL4 A2Kb tumor cells ( $1 \times 10^4$  cells/ well) as stimulators and A2 transgenic spleen cells as feeders ( $5 \times 10^5$  cells/ well) grown in the presence of 30U/ml IL-2. On day 14, cells were restimulated as before. On day 21, viable clones were  
25 isolated and maintained in culture. As shown in Figure 5, five of these clones demonstrated specific cytolytic reactivity against P501S-transduced Jurkat A2Kb targets. This data indicates that P1S#10 represents a naturally processed epitope of the P501S protein that is expressed in the context of the human HLA-A2.1 molecule.

## EXAMPLE 7

PRIMING OF CTL *IN VIVO* USING NAKED DNA IMMUNIZATION

## WITH A PROSTATE ANTIGEN

The prostate-specific antigen L1-12, as described above, is also referred  
5 to as P501S. HLA A2Kb Tg mice (provided by Dr L. Sherman, The Scripps Research  
Institute, La Jolla, CA) were immunized with 100 µg P501S in the vector VR1012  
either intramuscularly or intradermally. The mice were immunized three times, with a  
two week interval between immunizations. Two weeks after the last immunization,  
immune spleen cells were cultured with Jurkat A2Kb-P501S transduced stimulator  
10 cells. CTL lines were stimulated weekly. After two weeks of *in vitro* stimulation, CTL  
activity was assessed against P501S transduced targets. Two out of 8 mice developed  
strong anti-P501S CTL responses. These results demonstrate that P501S contains at  
least one naturally processed HLA-A2-restricted CTL epitope.

## 15 EXAMPLE 8

## ABILITY OF HUMAN T CELLS TO RECOGNIZE PROSTATE-SPECIFIC POLYPEPTIDES

This Example illustrates the ability of T cells specific for a prostate  
tumor polypeptide to recognize human tumor.

20 Human CD8<sup>+</sup> T cells were primed *in vitro* to the P2S-12 peptide (SEQ  
ID NO: 306) derived from P502S (also referred to as J1-17) using dendritic cells  
according to the protocol of Van Tsai et al. (*Critical Reviews in Immunology* 18:65-75,  
1998). The resulting CD8<sup>+</sup> T cell microcultures were tested for their ability to  
recognize the P2S-12 peptide presented by autologous fibroblasts or fibroblasts which  
25 were transduced to express the P502S gene in a γ-interferon ELISPOT assay (*see*  
Lalvani et al., *J. Exp. Med.* 186:859-865, 1997). Briefly, titrating numbers of T cells  
were assayed in duplicate on 10<sup>4</sup> fibroblasts in the presence of 3 µg/ml human β<sub>2</sub>-  
microglobulin and 1 µg/ml P2S-12 peptide or control E75 peptide. In addition, T cells  
were simultaneously assayed on autologous fibroblasts transduced with the P502S gene  
30 or as a control, fibroblasts transduced with HER-2/*neu*. Prior to the assay, the

fibroblasts were treated with 10 ng/ml  $\gamma$ -interferon for 48 hours to upregulate class I MHC expression. One of the microcultures (#5) demonstrated strong recognition of both peptide pulsed fibroblasts as well as transduced fibroblasts in a  $\gamma$ -interferon ELISPOT assay. Figure 2A demonstrates that there was a strong increase in the number of  $\gamma$ -interferon spots with increasing numbers of T cells on fibroblasts pulsed with the P2S-12 peptide (solid bars) but not with the control E75 peptide (open bars). This shows the ability of these T cells to specifically recognize the P2S-12 peptide. As shown in Figure 2B, this microculture also demonstrated an increase in the number of  $\gamma$ -interferon spots with increasing numbers of T cells on fibroblasts transduced to express the P502S gene but not the HER-2/*neu* gene. These results provide additional confirmatory evidence that the P2S-12 peptide is a naturally processed epitope of the P502S protein. Furthermore, this also demonstrates that there exists in the human T cell repertoire, high affinity T cells which are capable of recognizing this epitope. These T cells should also be capable of recognizing human tumors which express the P502S gene.

## EXAMPLE 9

### ELICITATION OF PROSTATE ANTIGEN-SPECIFIC CTL RESPONSES IN HUMAN BLOOD

20

This Example illustrates the ability of a prostate-specific antigen to elicit a CTL response in blood of normal humans.

Autologous dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal donors by growth for five days in RPMI medium containing 10% human serum, 50 ng/ml GMCSF and 30 ng/ml IL-4. Following culture, DC were infected overnight with recombinant P501S-expressing vaccinia virus at an M.O.I. of 5 and matured for 8 hours by the addition of 2 micrograms/ml CD40 ligand. Virus was inactivated by UV irradiation, CD8<sup>+</sup> cells were isolated by positive selection using magnetic beads, and priming cultures were initiated in 24-well plates. Following five stimulation cycles using autologous fibroblasts

retrovirally transduced to express P501S and CD80, CD8+ lines were identified that specifically produced interferon-gamma when stimulated with autologous P501S-transduced fibroblasts. The P501S-specific activity of cell line 3A-1 could be maintained following additional stimulation cycles on autologous B-LCL transduced with P501S. Line 3A-1 was shown to specifically recognize autologous B-LCL transduced to express P501S, but not EGFP-transduced autologous B-LCL, as measured by cytotoxicity assays ( $^{51}\text{Cr}$  release) and interferon-gamma production (Interferon-gamma Elispot; *see above and Lalvani et al., J. Exp. Med. 186:859-865, 1997*). The results of these assays are presented in Figures 6A and 6B.

10

## EXAMPLE 10

IDENTIFICATION OF A NATURALLY PROCESSED CTL EPITOPE CONTAINED WITHIN THE  
PROSTATE-SPECIFIC ANTIGEN P703P

The 9-mer peptide p5 (SEQ ID NO: 338) was derived from the P703P antigen (also referred to as P20). The p5 peptide is immunogenic in human HLA-A2 donors and is a naturally processed epitope. Antigen specific human CD8+ T cells can be primed following repeated *in vitro* stimulations with monocytes pulsed with p5 peptide. These CTL specifically recognize p5-pulsed and P703P-transduced target cells in both ELISPOT (as described above) and chromium release assays. Additionally, immunization of HLA-A2Kb transgenic mice with p5 leads to the generation of CTL lines which recognize a variety of HLA-A2Kb or HLA-A2 transduced target cells expressing P703P.

Initial studies demonstrating that p5 is a naturally processed epitope were done using HLA-A2Kb transgenic mice. HLA-A2Kb transgenic mice were immunized subcutaneously in the footpad with 100  $\mu\text{g}$  of p5 peptide together with 140  $\mu\text{g}$  of hepatitis B virus core peptide (a Th peptide) in Freund's incomplete adjuvant. Three weeks post immunization, spleen cells from immunized mice were stimulated *in vitro* with peptide-pulsed LPS blasts. CTL activity was assessed by chromium release assay five days after primary *in vitro* stimulation. Retrovirally transduced cells expressing the

control antigen P703P and HLA-A2Kb were used as targets. CTL lines that specifically recognized both p5-pulsed targets as well as P703P-expressing targets were identified.

Human *in vitro* priming experiments demonstrated that the p5 peptide is immunogenic in humans. Dendritic cells (DC) were differentiated from monocyte  
5 cultures derived from PBMC of normal human donors by culturing for five days in RPMI medium containing 10% human serum, 50 ng/ml human GM-CSF and 30 ng/ml human IL-4. Following culture, the DC were pulsed with 1 ug/ml p5 peptide and cultured with CD8+ T cell enriched PBMC. CTL lines were restimulated on a weekly basis with p5-pulsed monocytes. Five to six weeks after initiation of the CTL cultures,  
10 CTL recognition of p5-pulsed target cells was demonstrated. CTL were additionally shown to recognize human cells transduced to express P703P, demonstrating that p5 is a naturally processed epitope.

Studies identifying a further peptide epitope (referred to as peptide 4) derived from the prostate tumor-specific antigen P703P that is capable of being  
15 recognized by CD4 T cells on the surface of cells in the context of HLA class II molecules were carried out as follows. The amino acid sequence for peptide 4 is provided in SEQ ID NO: 781, with the corresponding cDNA sequence being provided in SEQ ID NO: 782.

Twenty 15-mer peptides overlapping by 10 amino acids and derived  
20 from the carboxy-terminal fragment of P703P were generated using standard procedures. Dendritic cells (DC) were derived from PBMC of a normal female donor using GM-CSF and IL-4 by standard protocols. CD4 T cells were generated from the same donor as the DC using MACS beads and negative selection. DC were pulsed overnight with pools of the 15-mer peptides, with each peptide at a final concentration  
25 of 0.25 microgram/ml. Pulsed DC were washed and plated at  $1 \times 10^4$  cells/well of 96-well V-bottom plates and purified CD4 T cells were added at  $1 \times 10^5$ /well. Cultures were supplemented with 60 ng/ml IL-6 and 10 ng/ml IL-12 and incubated at 37 °C. Cultures were restimulated as above on a weekly basis using DC generated and pulsed as above as antigen presenting cells, supplemented with 5 ng/ml IL-7 and 10 u/ml IL-2.  
30 Following 4 *in vitro* stimulation cycles, 96 lines (each line corresponding to one well) were tested for specific proliferation and cytokine production in response to the

stimulating pools with an irrelevant pool of peptides derived from mammaglobin being used as a control.

One line (referred to as 1-F9) was identified from pool #1 that demonstrated specific proliferation (measured by <sup>3</sup>H proliferation assays) and cytokine production (measured by interferon-gamma ELISA assays) in response to pool #1 of P703P peptides. This line was further tested for specific recognition of the peptide pool, specific recognition of individual peptides in the pool, and in HLA mismatch analyses to identify the relevant restricting allele. Line 1-F9 was found to specifically proliferate and produce interferon-gamma in response to peptide pool #1, and also to peptide 4 (SEQ ID NO: 781). Peptide 4 corresponds to amino acids 126-140 of SEQ ID NO: 327. Peptide titration experiments were conducted to assess the sensitivity of line 1-F9 for the specific peptide. The line was found to specifically respond to peptide 4 at concentrations as low as 0.25 ng/ml, indicating that the T cells are very sensitive and therefore likely to have high affinity for the epitope.

To determine the HLA restriction of the P703P response, a panel of antigen presenting cells (APC) was generated that was partially matched with the donor used to generate the T cells. The APC were pulsed with the peptide and used in proliferation and cytokine assays together with line 1-F9. APC matched with the donor at HLA-DRB0701 and HLA-DQB02 alleles were able to present the peptide to the T cells, indicating that the P703P-specific response is restricted to one of these alleles.

Antibody blocking assays were utilized to determine if the restricting allele was HLA-DR0701 or HLA-DQ02. The anti-HLA-DR blocking antibody L243 or an irrelevant isotype matched IgG2a were added to T cells and APC cultures pulsed with the peptide RMPTVLQCVNVSVVS (SEQ ID NO: 781) at 250 ng/ml. Standard interferon-gamma and proliferation assays were performed. Whereas the control antibody had no effect on the ability of the T cells to recognize peptide-pulsed APC, in both assays the anti-HLA-DR antibody completely blocked the ability of the T cells to specifically recognize peptide-pulsed APC.

To determine if the peptide epitope RMPTVLQCVNVSVVS (SEQ ID NO: 781) was naturally processed, the ability of line 1-F9 to recognize APC pulsed with recombinant P703P protein was examined. For these experiments a number of

recombinant P703P sources were utilized; *E. coli*-derived P703P, Pichia-derived P703P and baculovirus-derived P703P. Irrelevant protein controls used were *E. coli*-derived L3E (a lung-specific antigen) and baculovirus-derived mammaglobin. In interferon-gamma ELISA assays, line 1-F9 was able to efficiently recognize both *E. coli* forms of P703P as well as Pichia-derived recombinant P703P, while baculovirus-derived P703P was recognized less efficiently. Subsequent Western blot analysis revealed that the *E. coli* and Pichia P703P protein preparations were intact while the baculovirus P703P preparation was approximately 75% degraded. Thus, peptide RMPTVLQCVNVS VVS (SEQ ID NO: 781) from P703P is a naturally processed peptide epitope derived from P703P and presented to T cells in the context of HLA-DRB-0701

In further studies, twenty-four 15-mer peptides overlapping by 10 amino acids and derived from the N-terminal fragment of P703P (corresponding to amino acids 27-154 of SEQ ID NO: 525) were generated by standard procedures and their ability to be recognized by CD4 cells was determined essentially as described above. DC were pulsed overnight with pools of the peptides with each peptide at a final concentration of 10 microgram/ml. A large number of individual CD4 T cell lines (65/480) demonstrated significant proliferation and cytokine release (IFN-gamma) in response to the P703P peptide pools but not to a control peptide pool. The CD4 T cell lines which demonstrated specific activity were restimulated on the appropriate pool of P703P peptides and reassayed on the individual peptides of each pool as well as a peptide dose titration of the pool of peptides in a IFN-gamma release assay and in a proliferation assay.

Sixteen immunogenic peptides were recognized by the T cells from the entire set of peptide antigens tested. The amino acid sequences of these peptides are provided in SEQ ID NO: 799-814, with the corresponding cDNA sequences being provided in SEQ ID NO: 783-798, respectively. In some cases the peptide reactivity of the T cell line could be mapped to a single peptide, however some could be mapped to more than one peptide in each pool. Those CD4 T cell lines that displayed a representative pattern of recognition from each peptide pool with a reasonable affinity for peptide were chosen for further analysis (I-1A, -6A; II-4C, -5E; III-6E, IV-4B, -3F, -9B, -10F, V-5B, -4D, and -10F). These CD4 T cell lines were restimulated on the



appropriate individual peptide and reassayed on autologous DC pulsed with a truncated form of recombinant P703P protein made in *E. coli* (a.a. 96 - 254 of SEQ ID NO: 525), full-length P703P made in the baculovirus expression system, and a fusion between influenza virus NS1 and P703P made in *E. coli*. Of the T cell lines tested, line I-1A  
5 recognized specifically the truncated form of P703P (*E. coli*) but no other recombinant form of P703P. This line also recognized the peptide used to elicit the T cells. Line 2-4C recognized the truncated form of P703P (*E. coli*) and the full length form of P703P made in baculovirus, as well as peptide. The remaining T cell lines tested were either peptide-specific only (II-5E, II-6F, IV-4B, IV-3F, IV-9B, IV-10F, V-5B and V-4D) or  
10 were non-responsive to any antigen tested (V-10F). These results demonstrate that the peptide sequence RPLLANDLMLIKLDE (SEQ ID NO: 814; corresponding to a.a. 110-124 of SEQ ID NO: 525) recognized by the T cell line I-1A, and the peptide sequences SVSESDTIRSISIAS (SEQ ID NO: 811; corresponding to a.a. 125-139 of SEQ ID NO: 525) and ISIASQCPTAGNSCL (SEQ ID NO: 810; corresponding to a.a. 135-149 of  
15 SEQ ID NO: 525) recognized by the T cell line II-4C may be naturally processed epitopes of the P703P protein.

In further studies, forty 15-mer peptides overlapping by 10 amino acids and derived spanning amino acids 47 to 254 of P703P (SEQ ID NO: 525) were generated by standard procedures and their ability to be recognized by CD4 cells was  
20 determined essentially as described above. DC were prepared from PBMC of a donor having distinct HLA DR and DQ alleles from that used in previous experiments. DC were pulsed overnight with pools of the peptides with each peptide at a final concentration of 0.25 microgram/ml, and each pool containing 10 peptides. Twelve lines were identified that demonstrated specific proliferation and cytokine production  
25 (measured in gamma-interferon ELISA assays) in response to the stimulating peptide pool. These lines were further tested for specific recognition of the peptide pool, specific recognition of individual peptides in the pool, and specific recognition of recombinant P703P protein. Lines 3A5H and 3A9H specifically proliferated and produced gamma-interferon in response to recombinant protein and one individual  
30 peptide as well as the peptide pool. Following re-stimulation on targets loaded with the specific peptide, only 3A9H responded specifically to targets exposed to lysates of

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fibroblasts infected adenovirus expressing full-length P703P. These results indicates that the line 3A9H can respond to antigenic peptide derived from protein synthesized in mammalian cells. The peptide to which the specific CD4 line responded correspond to amino acids 155-170 of P703P (SEQ ID NO: 943). The DNA sequence for this peptide  
5 is provided in SEQ ID NO: 942.

### EXAMPLE 11

#### EXPRESSION OF A BREAST TUMOR-DERIVED ANTIGEN IN PROSTATE

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Isolation of the antigen B305D from breast tumor by differential display is described in US Patent Application No. 08/700,014, filed August 20, 1996. Several different splice forms of this antigen were isolated. The determined cDNA sequences for these splice forms are provided in SEQ ID NO: 366-375, with the predicted amino  
15 acid sequences corresponding to the sequences of SEQ ID NO: 292, 298 and 301-303 being provided in SEQ ID NO: 299-306, respectively. In further studies, a splice variant of the cDNA sequence of SEQ ID NO: 366 was isolated which was found to contain an additional guanine residue at position 884 (SEQ ID NO: 530), leading to a frameshift in the open reading frame. The determined DNA sequence of this ORF is  
20 provided in SEQ ID NO: 531. This frameshift generates a protein sequence (provided in SEQ ID NO: 532) of 293 amino acids that contains the C-terminal domain common to the other isoforms of B305D but that differs in the N-terminal region.

The expression levels of B305D in a variety of tumor and normal tissues were examined by real time PCR and by Northern analysis. The results indicated that  
25 B305D is highly expressed in breast tumor, prostate tumor, normal prostate and normal testes, with expression being low or undetectable in all other tissues examined (colon tumor, lung tumor, ovary tumor, and normal bone marrow, colon, kidney, liver, lung, ovary, skin, small intestine, stomach). Using real-time PCR on a panel of prostate tumors, expression of B305D in prostate tumors was shown to increase with increasing

Gleason grade, demonstrating that expression of B305D increases as prostate cancer progresses.

## EXAMPLE 12

### 5 GENERATION OF HUMAN CTL *IN VITRO* USING WHOLE GENE PRIMING AND STIMULATION TECHNIQUES WITH THE PROSTATE-SPECIFIC ANTIGEN P501S

Using *in vitro* whole-gene priming with P501S-vaccinia infected DC (see, for example, Yee et al, *The Journal of Immunology*, 157(9):4079-86, 1996),  
10 human CTL lines were derived that specifically recognize autologous fibroblasts transduced with P501S (also known as L1-12), as determined by interferon- $\gamma$  ELISPOT analysis as described above. Using a panel of HLA-mismatched B-LCL lines transduced with P501S, these CTL lines were shown to be likely restricted to HLAB class I allele. Specifically, dendritic cells (DC) were differentiated from monocyte  
15 cultures derived from PBMC of normal human donors by growing for five days in RPMI medium containing 10% human serum, 50 ng/ml human GM-CSF and 30 ng/ml human IL-4. Following culture, DC were infected overnight with recombinant P501S vaccinia virus at a multiplicity of infection (M.O.I) of five, and matured overnight by the addition of 3  $\mu$ g/ml CD40 ligand. Virus was inactivated by UV irradiation. CD8+  
20 T cells were isolated using a magnetic bead system, and priming cultures were initiated using standard culture techniques. Cultures were restimulated every 7-10 days using autologous primary fibroblasts retrovirally transduced with P501S and CD80. Following four stimulation cycles, CD8+ T cell lines were identified that specifically produced interferon- $\gamma$  when stimulated with P501S and CD80-transduced autologous  
25 fibroblasts. A panel of HLA-mismatched B-LCL lines transduced with P501S were generated to define the restriction allele of the response. By measuring interferon- $\gamma$  in an ELISPOT assay, the P501S specific response was shown to be likely restricted by HLA B alleles. These results demonstrate that a CD8+ CTL response to P501S can be elicited.

To identify the epitope(s) recognized, cDNA encoding P501S was fragmented by various restriction digests, and sub-cloned into the retroviral expression vector pBIB-KS. Retroviral supernatants were generated by transfection of the helper packaging line Phoenix-Ampho. Supernatants were then used to transduce Jurkat/A2Kb cells for CTL screening. CTL were screened in IFN-gamma ELISPOT assays against these A2Kb targets transduced with the "library" of P501S fragments. Initial positive fragments P501S/H3 and P501S/F2 were sequenced and found to encode amino acids 106-553 and amino acids 136-547, respectively, of SEQ ID NO: 113. A truncation of H3 was made to encode amino acid residues 106-351 of SEQ ID NO: 113, which was unable to stimulate the CTL, thus localizing the epitope to amino acid residues 351-547. Additional fragments encoding amino acids 1-472 (Fragment A) and amino acids 1-351 (Fragment B) were also constructed. Fragment A but not Fragment B stimulated the CTL thus localizing the epitope to amino acid residues 351-472. Overlapping 20-mer and 18-mer peptides representing this region were tested by pulsing Jurkat/A2Kb cells versus CTL in an IFN-gamma assay. Only peptides P501S-369(20) and P501S-369(18) stimulated the CTL. Nine-mer and 10-mer peptides representing this region were synthesized and similarly tested. Peptide P501S-370 (SEQ ID NO: 539) was the minimal 9-mer giving a strong response. Peptide P501S-376 (SEQ ID NO: 540) also gave a weak response, suggesting that it might represent a cross-reactive epitope.

In subsequent studies, the ability of primary human B cells transduced with P501S to prime MHC class I-restricted, P501S-specific, autologous CD8 T cells was examined. Primary B cells were derived from PBMC of a homozygous HLA-A2 donor by culture in CD40 ligand and IL-4, transduced at high frequency with recombinant P501S in the vector pBIB, and selected with blastocidin-S. For *in vitro* priming, purified CD8<sup>+</sup> T cells were cultured with autologous CD40 ligand + IL-4 derived, P501S-transduced B cells in a 96-well microculture format. These CTL microcultures were re-stimulated with P501S-transduced B cells and then assayed for specificity. Following this initial screen, microcultures with significant signal above background were cloned on autologous EBV-transformed B cells (BLCL), also

transduced with P501S. Using IFN-gamma ELISPOT for detection, several of these CD8 T cell clones were found to be specific for P501S, as demonstrated by reactivity to BLCL/P501S but not BLCL transduced with control antigen. It was further demonstrated that the anti-P501S CD8 T cell specificity is HLA-A2-restricted. First, antibody blocking experiments with anti-HLA-A,B,C monoclonal antibody (W6.32), anti-HLA-B,C monoclonal antibody (B1.23.2) and a control monoclonal antibody showed that only the anti-HLA-A,B,C antibody blocked recognition of P501S-expressing autologous BLCL. Secondly, the anti-P501S CTL also recognized an HLA-A2 matched, heterologous BLCL transduced with P501S, but not the corresponding EGFP transduced control BLCL.

A naturally processed, CD8, class I-restricted peptide epitope of P501S was identified as follows. Dendritic Cells (DC) were isolated by Percol gradient followed by differential adherence, and cultured for 5 days in the presence of RPMI medium containing 1% human serum, 50ng/ml GM-CSF and 30ng/ml IL-4. Following culture, DC were infected for 24 hours with P501S-expressing adenovirus at an MOI of 10 and matured for an additional 24 hours by the addition of 2ug/ml CD40 ligand. CD8 cells were enriched for by the subtraction of CD4+, CD14+ and CD16+ populations from PBMC with magnetic beads. Priming cultures containing 10,000 P501S-expressing DC and 100,000 CD8+ T cells per well were set up in 96-well V-bottom plates with RPMI containing 10% human serum, 5ng/ml IL-12 and 10ng/ml IL-6. Cultures were stimulated every 7 days using autologous fibroblasts retrovirally transduced to express P501S and CD80, and were treated with IFN-gamma for 48-72 hours to upregulate MHC Class I expression. 10u/ml IL-2 was added at the time of stimulation and on days 2 and 5 following stimulation. Following 4 stimulation cycles, one P501S-specific CD8+ T cell line (referred to as 2A2) was identified that produced IFN-gamma in response to IFN-gamma-treated P501S/CD80 expressing autologous fibroblasts, but not in response to IFN-gamma-treated P703P/CD80 expressing autologous fibroblasts in a  $\gamma$ -IFN Elispot assay. Line 2A2 was cloned in 96-well plates with 0.5 cell/well or 2 cells/well in the presence of 75,000 PBMC/well, 10,000 B-LCL/well, 30ng/ml OKT3 and 50u/ml IL-2. Twelve clones were isolated that showed strong P501S specificity in response to transduced fibroblasts.

Fluorescence activated cell sorting (FACS) analysis was performed on P501S-specific clones using CD3-, CD4- and CD8-specific antibodies conjugated to PercP, FITC and PE respectively. Consistent with the use of CD8 enriched T cells in the priming cultures, P5401S-specific clones were determined to be CD3+, CD8+ and  
5 CD4-.

To identify the relevant P501S epitope recognized by P501S specific CTL, pools of 18-20 mer or 30-mer peptides that spanned the majority of the amino acid sequence of P501S were loaded onto autologous B-LCL and tested in  $\gamma$ -IFN Elispot assays for the ability to stimulate two P501S-specific CTL clones, referred to as 4E5  
10 and 4E7. One pool, composed of five 18-20 mer peptides that spanned amino acids 411-486 of P501S (SEQ ID NO: 113), was found to be recognized by both P501S-specific clones. To identify the specific 18-20 mer peptide recognized by the clones, each of the 18-20 mer peptides that comprised the positive pool were tested individually in  $\gamma$ -IFN Elispot assays for the ability to stimulate the two P501S-specific CTL clones, 4E5 and  
15 4E7. Both 4E5 and 4E7 specifically recognized one 20-mer peptide (SEQ ID NO: 853; cDNA sequence provided in SEQ ID NO: 854) that spanned amino acids 453-472 of P501S. Since the minimal epitope recognized by CD8+ T cells is almost always either a 9 or 10-mer peptide sequence, 10-mer peptides that spanned the entire sequence of SEQ ID NO: 853 were synthesized that differed by 1 amino acid. Each of these 10-mer  
20 peptides was tested for the ability to stimulate two P501S-specific clones, (referred to as 1D5 and 1E12). One 10-mer peptide (SEQ ID NO: 855; cDNA sequence provided in SEQ ID NO: 856) was identified that specifically stimulated the P501S-specific clones. This epitope spans amino acids 463-472 of P501S. This sequence defines a minimal 10-mer epitope from P501S that can be naturally processed and to which CTL responses  
25 can be identified in normal PBMC. Thus, this epitope is a candidate for use as a vaccine moiety, and as a therapeutic and/or diagnostic reagent for prostate cancer.

To identify the class I restriction element for the P501S-derived sequence of SEQ ID NO: 855, HLA blocking and mismatch analyses were performed. In  $\gamma$ -IFN Elispot assays, the specific response of clones 4A7 and 4E5 to P501S-transduced  
30 autologous fibroblasts was blocked by pre-incubation with 25ug/ml W6/32 (pan-Class I blocking antibody) and B1.23.2 (HLA-B/C blocking antibody). These results

demonstrate that the SEQ ID NO: 855-specific response is restricted to an HLA-B or HLA-C allele.

For the HLA mismatch analysis, autologous B-LCL (HLA-A1,A2,B8,B51, Cw1, Cw7) and heterologous B-LCL (HLA-A2,A3,B18,B51,Cw5,Cw14) that share the HLAB51 allele were pulsed for one hour with 20ug/ml of peptide of SEQ ID NO: 855, washed, and tested in  $\gamma$ -IFN Elispot assays for the ability to stimulate clones 4A7 and 4E5. Antibody blocking assays with the B1.23.2 (HLA-B/C blocking antibody) were also performed. SEQ ID NO: 855-specific response was detected using both the autologous (D326) and heterologous (D107) B-LCL, and furthermore the responses were blocked by pre-incubation with 25ug/ml of B1.23.2 HLA-B/C blocking antibody. Together these results demonstrate that the P501S-specific response to the peptide of SEQ ID NO: 855 is restricted to the HLA-B51 class I allele. Molecular cloning and sequence analysis of the HLA-B51 allele from D3326 revealed that the HLA-B51 subtype of D326 is HLA-B51011.

Based on the 10-mer P501S-derived epitope of SEQ ID NO: 855, two 9-mers with the sequences of SEQ ID NO: 857 and 858 were synthesized and tested in Elispot assays for the ability to stimulate two P501S-specific CTL clones derived from line 2A2. The 10-mer peptide of SEQ ID NO: 855, as well as the 9-mer peptide of SEQ ID NO: 858, but not the 9-mer peptide of SEQ ID NO: 857, were capable of stimulating the P501S-specific CTL to produce IFN-gamma. These results demonstrate that the peptide of SEQ ID NO: 858 is a 9-mer P501S-derived epitope recognized by P501S-specific CTL. The DNA sequence encoding the epitope of SEQ ID NO: 858 is provided in SEQ ID NO: 859.

To identify the class I restricting allele for the P501S-derived peptide of SEQ ID NO: 855 and 858 specific response, each of the HLA B and C alleles were cloned from the donor used in the *in vitro* priming experiment. Sequence analysis indicated that the relevant alleles were HLA-B8, HLA-B51, HLA-Cw01 and HLA-Cw07. Each of these alleles were subcloned into an expression vector and co-transfected together with the P501S gene into VA-13 cells. Transfected VA-13 cells were then tested for the ability to specifically stimulate the P501S-specific CTL in ELISPOT assays. VA-13 cells transfected with P501S and HLA-B51 were capable of

stimulating the P501S-specific CTL to secrete gamma-IFN. VA-13 cells transfected with HLA-B51 alone or P501S + the other HLA-alleles were not capable of stimulating the P501S-specific CTL. These results demonstrate that the restricting allele for the P501S-specific response is the HLAB51 allele. Sequence analysis revealed that the  
5 subtype of the relevant restricting allele is HLA-B51011.

To determine if the P501S-specific CTL could recognize prostate tumor cells that express P501S, the P501S-positive lines LnCAP and CRL2422 (both expressing "moderate" amounts of P501S mRNA and protein), and PC-3 (expressing low amounts of P501S mRNA and protein), plus the P501S-negative cell line DU-145  
10 were retrovirally transduced with the HLA-B51011 allele that was cloned from the donor used to generate the P501S-specific CTL. HLA-B51011- or EGFP-transduced and selected tumor cells were treated with gamma-interferon and androgen (to upregulate stimulatory functions and P501S, respectively) and used in gamma-interferon Elispot assays with the P501S-specific CTL clones 4E5 and 4E7. Untreated  
15 cells were used as a control.

Both 4E5 and 4E7 efficiently and specifically recognized LnCAP and CRL2422 cells that were transduced with the HLA-B51011 allele, but not the same cell lines transduced with EGFP. Additionally, both CTL clones specifically recognized PC-3 cells transduced with HLA-B51011, but not the P501S-negative tumor cell line  
20 DU-145. Treatment with gamma-interferon or androgen did not enhance the ability of CTL to recognize tumor cells. These results demonstrate that P501S-specific CTL, generated by *in vitro* whole gene priming, specifically and efficiently recognize prostate tumor cell lines that express P501S.

A naturally processed CD4 epitope of P501S was identified as follows.

25 CD4 cells specific for P501S were prepared as described above. A series of 16 overlapping peptides were synthesized that spanned approximately 50% of the amino terminal portion of the P501S gene (amino acids 1- 325 of SEQ ID NO: 113). For priming, peptides were combined into pools of 4 peptides, pulsed at 4 µg/ml onto dendritic cells (DC) for 24 hours, with TNF-alpha. DC were then washed and mixed  
30 with negatively selected CD4+ T cells in 96 well U-bottom plates. Cultures were re-stimulated weekly on fresh DC loaded with peptide pools. Following a total of 4



stimulation cycles, cells were rested for an additional week and tested for specificity to APC pulsed with peptide pools using  $\gamma$ -IFN ELISA and proliferation assays. For these assays, adherent monocytes loaded with either the relevant peptide pool at 4 $\mu$ g/ml or an irrelevant peptide at  $\mu$ g/ml were used as APC. T cell lines that demonstrated either  
5 specific cytokine secretion or proliferation were then tested for recognition of individual peptides that were present in the pool. T cell lines could be identified from pools A and B that recognized individual peptides from these pools.

From pool A, lines AD9 and AE10 specifically recognized peptide 1 (SEQ ID NO: 862), and line AF5 recognized peptide 39 (SEQ ID NO: 861). From pool  
10 B, line BC6 could be identified that recognized peptide 58 (SEQ ID NO: 860). Each of these lines were stimulated on the specific peptide and tested for specific recognition of the peptide in a titration assay as well as cell lysates generated by infection of HEK 293 cells with adenovirus expressing either P501S or an irrelevant antigen. For these assays, APC-adherent monocytes were pulsed with either 10, 1, or 0.1  $\mu$ g/ml individual P501S  
15 peptides, and DC were pulsed overnight with a 1:5 dilution of adenovirally infected cell lysates. Lines AD9, AE10 and AF5 retained significant recognition of the relevant P501S-derived peptides even at 0.1 mg/ml. Furthermore, line AD9 demonstrated significant (8.1 fold stimulation index) specific activity for lysates from adenovirus-P501S infected cells. These results demonstrate that high affinity CD4 T cell lines can  
20 be generated toward P501S-derived epitopes, and that at least a subset of these T cells specific for the P501S derived sequence of SEQ ID NO: 862 are specific for an epitope that is naturally processed by human cells. The DNA sequences encoding the amino acid sequences of SEQ ID NO: 860-862 are provided in SEQ ID NO: 863-865, respectively.

25 To further characterize the P501S-specific activity of AD9, the line was cloned using anti-CD3. Three clones, referred to as 1A1, 1A9 and 1F5, were identified that were specific for the P501S-1 peptide (SEQ ID NO: 862). To determine the HLA restriction allele for the P501S-specific response, each of these clones was tested in class II antibody blocking and HLA mismatch assays using proliferation and gamma-  
30 interferon assays. In antibody blocking assays and measuring gamma-interferon production using ELISA assays, the ability of all three clones to recognize peptide

pulsed APC was specifically blocked by co-incubation with either a pan-class II blocking antibody or a HLA-DR blocking antibody, but not with a HLA-DQ or an irrelevant antibody. Proliferation assays performed simultaneously with the same cells confirmed these results. These data indicate that the P501S-specific response of the clones is restricted by an HLA-DR allele. Further studies demonstrated that the restricting allele for the P501S-specific response is HLA-DRB1501.

### EXAMPLE 13

#### IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS

#### BY MICROARRAY ANALYSIS

This Example describes the isolation of certain prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library as described above was screened using microarray analysis to identify clones that display at least a three fold over-expression in prostate tumor and/or normal prostate tissue, as compared to non-prostate normal tissues (not including testis). 372 clones were identified, and 319 were successfully sequenced. Table I presents a summary of these clones, which are shown in SEQ ID NOs:385-400. Of these sequences SEQ ID NOs:386, 389, 390 and 392 correspond to novel genes, and SEQ ID NOs: 393 and 396 correspond to previously identified sequences. The others (SEQ ID NOs:385, 387, 388, 391, 394, 395 and 397-400) correspond to known sequences, as shown in Table I.

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Table ISummary of Prostate Tumor Antigens

Known Genes	Previously Identified Genes	Novel Genes
T-cell gamma chain	P504S	23379 (SEQ ID NO:389)
Kallikrein	P1000C	23399 (SEQ ID NO:392)
Vector	P501S	23320 (SEQ ID NO:386)
CGI-82 protein mRNA (23319; SEQ ID NO:385)	P503S	23381 (SEQ ID NO:390)
PSA	P510S	
Ald. 6 Dehyd.	P784P	
L-iditol-2 dehydrogenase (23376; SEQ ID NO:388)	P502S	
Ets transcription factor PDEF (22672; SEQ ID NO:398)	P706P	
hTGR (22678; SEQ ID NO:399)	19142.2, bangur.seq (22621; SEQ ID NO:396)	
KIAA0295(22685; SEQ ID NO:400)	5566.1 Wang (23404; SEQ ID NO:393)	
Prostatic Acid Phosphatase(22655; SEQ ID NO:397)	P712P	
transglutaminase (22611; SEQ ID NO:395)	P778P	
HDLBP (23508; SEQ ID NO:394)		
CGI-69 Protein(23367; SEQ ID NO:387)		
KIAA0122(23383; SEQ ID NO:391)		
TEEG		

CGI-82 showed 4.06 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 43% of prostate tumors, 25% normal prostate, not detected in other normal tissues tested. L-iditol-2 dehydrogenase showed 4.94 fold over-expression in prostate tissues as compared to  
5 other normal tissues tested. It was over-expressed in 90% of prostate tumors, 100% of normal prostate, and not detected in other normal tissues tested. Ets transcription factor PDEF showed 5.55 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 47% prostate tumors, 25% normal prostate and not detected in other normal tissues tested. hTGR1 showed 9.11 fold over-expression in  
10 prostate tissues as compared to other normal tissues tested. It was over-expressed in 63% of prostate tumors and is not detected in normal tissues tested including normal prostate. KIAA0295 showed 5.59 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 47% of prostate tumors, low to undetectable in normal tissues tested including normal prostate tissues. Prostatic acid  
15 phosphatase showed 9.14 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 67% of prostate tumors, 50% of normal prostate, and not detected in other normal tissues tested. Transglutaminase showed 14.84 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 30% of prostate tumors, 50% of normal prostate, and is  
20 not detected in other normal tissues tested. High density lipoprotein binding protein (HDLBP) showed 28.06 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors, 75% of normal prostate, and is undetectable in all other normal tissues tested. CGI-69 showed 3.56 fold over-expression in prostate tissues as compared to other normal tissues tested. It is  
25 a low abundant gene, detected in more than 90% of prostate tumors, and in 75% normal prostate tissues. The expression of this gene in normal tissues was very low. KIAA0122 showed 4.24 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 57% of prostate tumors, it was undetectable in all normal tissues tested including normal prostate tissues. 19142.2  
30 bangur showed 23.25 fold over-expression in prostate tissues as compared to other

normal tissues tested. It was over-expressed in 97% of prostate tumors and 100% of normal prostate. It was undetectable in other normal tissues tested. 5566.1 Wang showed 3.31 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors, 75% normal prostate and was also over-expressed in normal bone marrow, pancreas, and activated PBMC. Novel clone 23379 (also referred to as P553S) showed 4.86 fold over-expression in prostate tissues as compared to other normal tissues tested. It was detectable in 97% of prostate tumors and 75% normal prostate and is undetectable in all other normal tissues tested. Novel clone 23399 showed 4.09 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 27% of prostate tumors and was undetectable in all normal tissues tested including normal prostate tissues. Novel clone 23320 showed 3.15 fold over-expression in prostate tissues as compared to other normal tissues tested. It was detectable in all prostate tumors and 50% of normal prostate tissues. It was also expressed in normal colon and trachea. Other normal tissues do not express this gene at high level.

Subsequent full-length cloning studies on P553S, using standard techniques, revealed that this clone is an incomplete spliced form of P501S. The determined cDNA sequences for four splice variants of P553S are provided in SEQ ID NO: 702-705. An amino acid sequence encoded by SEQ ID NO: 705 is provided in SEQ ID NO: 706. The cDNA sequence of SEQ ID NO: 702 was found to contain two open reading frames (ORFs). The amino acid sequences encoded by these two ORFs are provided in SEQ ID NO: 707 and 708.

#### EXAMPLE 14

##### IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS BY ELECTRONIC SUBTRACTION

This Example describes the use of an electronic subtraction technique to identify prostate-specific antigens.

Potential prostate-specific genes present in the GenBank human EST database were identified by electronic subtraction (similar to that described by Vasmatazsis et al., *Proc. Natl. Acad. Sci. USA* 95:300-304, 1998). The sequences of EST clones (43,482) derived from various prostate libraries were obtained from the GenBank public human EST database. Each prostate EST sequence was used as a query sequence in a BLASTN (National Center for Biotechnology Information) search against the human EST database. All matches considered identical (length of matching sequence >100 base pairs, density of identical matches over this region > 70%) were grouped (aligned) together in a cluster. Clusters containing more than 200 ESTs were discarded since they probably represented repetitive elements or highly expressed genes such as those for ribosomal proteins. If two or more clusters shared common ESTs, those clusters were grouped together into a "supercluster," resulting in 4,345 prostate superclusters.

Records for the 479 human cDNA libraries represented in the GenBank release were downloaded to create a database of these cDNA library records. These 479 cDNA libraries were grouped into three groups: Plus (normal prostate and prostate tumor libraries, and breast cell line libraries, in which expression was desired), Minus (libraries from other normal adult tissues, in which expression was not desirable), and Other (libraries from fetal tissue, infant tissue, tissues found only in women, non-prostate tumors and cell lines other than prostate cell lines, in which expression was considered to be irrelevant). A summary of these library groups is presented in Table II.

Table IIProstate cDNA Libraries and ESTs

Library	# of Libraries	# of ESTs
Plus	25	43,482
Normal	11	18,875
Tumor	11	21,769
Cell lines	3	2,838
Minus	166	
Other	287	

5            Each supercluster was analyzed in terms of the ESTs within the supercluster. The tissue source of each EST clone was noted and used to classify the superclusters into four groups: Type 1- EST clones found in the Plus group libraries only; no expression detected in Minus or Other group libraries; Type 2- EST clones derived from the Plus and Other group libraries only; no expression detected in the

10 Minus group; Type 3- EST clones derived from the Plus, Minus and Other group libraries, but the number of ESTs derived from the Plus group is higher than in either the Minus or Other groups; and Type 4- EST clones derived from Plus, Minus and Other group libraries, but the number derived from the Plus group is higher than the number derived from the Minus group. This analysis identified 4,345 breast clusters

15 (see Table III). From these clusters, 3,172 EST clones were ordered from Research Genetics, Inc., and were received as frozen glycerol stocks in 96-well plates.

Table IIIProstate Cluster Summary

Type	# of Superclusters	# of ESTs Ordered
1	688	677
2	2899	2484
3	85	11
4	673	0
Total	4345	3172

5           The EST clone inserts were PCR-amplified using amino-linked PCR primers for Synteni microarray analysis. When more than one PCR product was obtained for a particular clone, that PCR product was not used for expression analysis. In total, 2,528 clones from the electronic subtraction method were analyzed by microarray analysis to identify electronic subtraction breast clones that had high levels  
10 of tumor vs. normal tissue mRNA. Such screens were performed using a Synteni (Palo Alto, CA) microarray, according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA* 93:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA* 94:2150-2155, 1997). Within these analyses, the clones were arrayed on the chip, which was then probed with fluorescent probes  
15 generated from normal and tumor prostate cDNA, as well as various other normal tissues. The slides were scanned and the fluorescence intensity was measured.

Clones with an expression ratio greater than 3 (*i.e.*, the level in prostate tumor and normal prostate mRNA was at least three times the level in other normal tissue mRNA) were identified as prostate tumor-specific sequences (Table IV). The  
20 sequences of these clones are provided in SEQ ID NO: 401-453, with certain novel sequences shown in SEQ ID NO: 407, 413, 416-419, 422, 426, 427 and 450.



Table IV

Prostate-tumor Specific Clones

SEQ ID NO.	Sequence Designation	Comments
401	22545	previously identified P1000C
402	22547	previously identified P704P
403	22548	known
404	22550	known
405	22551	PSA
406	22552	prostate secretory protein 94
407	22553	novel
408	22558	previously identified P509S
409	22562	glandular kallikrein
410	22565	previously identified P1000C
411	22567	PAP
412	22568	B1006C (breast tumor antigen)
413	22570	novel
414	22571	PSA
415	22572	previously identified P706P
416	22573	novel
417	22574	novel
418	22575	novel
419	22580	novel
420	22581	PAP
421	22582	prostatic secretory protein 94
422	22583	novel
423	22584	prostatic secretory protein 94
424	22585	prostatic secretory protein 94
425	22586	known
426	22587	novel
427	22588	novel
428	22589	PAP
429	22590	known
430	22591	PSA
431	22592	known
432	22593	Previously identified P777P
433	22594	T cell receptor gamma chain
434	22595	Previously identified P705P
435	22596	Previously identified P707P
436	22847	PAP
437	22848	known
438	22849	prostatic secretory protein 57

439	22851	PAP
440	22852	PAP
441	22853	PAP
442	22854	previously identified P509S
443	22855	previously identified P705P
444	22856	previously identified P774P
445	22857	PSA
446	23601	previously identified P777P
447	23602	PSA
448	23605	PSA
449	23606	PSA
450	23612	novel
451	23614	PSA
452	23618	previously identified P1000C
453	23622	previously identified P705P

Further studies on the clone of SEQ ID NO: 407 (also referred to as P1020C) led to the isolation of an extended cDNA sequence provided in SEQ ID NO: 591. This extended cDNA sequence was found to contain an open reading frame that  
5 encodes the predicted amino acid sequence of SEQ ID NO: 592. The P1020C cDNA and amino acid sequences were found to show some similarity to the human endogenous retroviral HERV-K pol gene and protein.

#### EXAMPLE 15

##### 10 FURTHER IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS BY MICROARRAY ANALYSIS

This Example describes the isolation of additional prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library as described above  
15 was screened using microarray analysis to identify clones that display at least a three fold over-expression in prostate tumor and/or normal prostate tissue, as compared to non-prostate normal tissues (not including testis). 142 clones were identified and sequenced. Certain of these clones are shown in SEQ ID NO: 454-467. Of these sequences, SEQ ID NO: 459-460 represent novel genes. The others (SEQ ID NO: 454-  
20 458 and 461-467) correspond to known sequences. Comparison of the determined

cDNA sequence of SEQ ID NO: 461 with sequences in the Genbank database using the BLAST program revealed homology to the previously identified transmembrane protease serine 2 (TMPRSS2). The full-length cDNA sequence for this clone is provided in SEQ ID NO: 894, with the corresponding amino acid sequence being  
5 provided in SEQ ID NO: 895. The cDNA sequence encoding the first 209 amino acids of TMPRSS2 is provided in SEQ ID NO: 896, with the first 209 amino acids being provided in SEQ ID NO: 897.

The sequence of SEQ ID NO: 462 (referred to as P835P) was found to correspond to the previously identified clone FLJ13518 (Accession AK023643; SEQ ID  
10 NO: 917), which had no associated open reading frame (ORF). This clone was used to search the Geneseq DNA database and matched a clone previously identified as a G protein-coupled receptor protein (DNA Geneseq Accession A09351; amino acid Geneseq Accession Y92365), that is characterized by the presence of seven transmembrane domains. The sequences of fragments between these domains are  
15 provided in SEQ ID NO: 921-928, with SEQ ID NO: 921, 923, 925 and 927 representing extracellular domains and SEQ ID NO: 922, 924, 926 and 928 representing intracellular domains. SEQ ID NO: 921-928 represent amino acids 1-28, 53-61, 83-103, 124-143, 165-201, 226-238, 263-272 and 297-381, respectively, of P835P. The full-length cDNA sequence for P835P is provided in SEQ ID NO: 916. The cDNA  
20 sequence of the open reading frame for P835P, including stop codon, is provided in SEQ ID NO: 918, with the open reading frame without stop codon being provided in SEQ ID NO: 919 and the corresponding amino acid sequence being provided in SEQ ID NO: 920.

25

## EXAMPLE 16

### FURTHER CHARACTERIZATION OF PROSTATE-SPECIFIC ANTIGEN P710P

This Example describes the full length cloning of P710P.

The prostate cDNA library described above was screened with the P710P  
30 fragment described above. One million colonies were plated on LB/Ampicillin plates.

Nylon membrane filters were used to lift these colonies, and the cDNAs picked up by these filters were then denatured and cross-linked to the filters by UV light. The P710P fragment was radiolabeled and used to hybridize with the filters. Positive cDNA clones were selected and their cDNAs recovered and sequenced by an automatic Perkin Elmer/Applied Biosystems Division Sequencer. Four sequences were obtained, and are presented in SEQ ID NO: 468-471. These sequences appear to represent different splice variants of the P710P gene. Subsequent comparison of the cDNA sequences of P710P with those in Genbank revealed homology to the DD3 gene (Genbank accession numbers AF103907 & AF103908). The cDNA sequence of DD3 is provided in SEQ ID NO: 690.

#### EXAMPLE 17

##### PROTEIN EXPRESSION OF PROSTATE-SPECIFIC ANTIGENS

This example describes the expression and purification of prostate-specific antigens in *E. coli*, baculovirus and mammalian cells.

##### a) Expression of P501S in *E. coli*

Expression of the full-length form of P501S was attempted by first cloning P501S without the leader sequence (amino acids 36-553 of SEQ ID NO: 113) downstream of the first 30 amino acids of the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 484) in pET17b. Specifically, P501S DNA was used to perform PCR using the primers AW025 (SEQ ID NO: 485) and AW003 (SEQ ID NO: 486). AW025 is a sense cloning primer that contains a HindIII site. AW003 is an antisense cloning primer that contains an EcoRI site. DNA amplification was performed using 5 µl 10X Pfu buffer, 1 µl 20 mM dNTPs, 1 µl each of the PCR primers at 10 µM concentration, 40 µl water, 1 µl Pfu DNA polymerase (Stratagene, La Jolla, CA) and 1 µl DNA at 100 ng/µl. Denaturation at 95°C was performed for 30 sec, followed by 10 cycles of 95°C for 30 sec, 60°C for 1 min and by 72°C for 3 min. 20 cycles of 95°C for 30 sec, 65°C for 1 min and by 72°C for 3 min, and lastly by 1 cycle of 72°C for 10 min. The PCR product was

cloned to Ra12m/pET17b using HindIII and EcoRI. The sequence of the resulting fusion construct (referred to as Ra12-P501S-F) was confirmed by DNA sequencing.

The fusion construct was transformed into BL21(DE3)pLysE, pLysS and CodonPlus *E. coli* (Stratagene) and grown overnight in LB broth with kanamycin. The  
5 resulting culture was induced with IPTG. Protein was transferred to PVDF membrane and blocked with 5% non-fat milk (in PBS-Tween buffer), washed three times and incubated with mouse anti-His tag antibody (Clontech) for 1 hour. The membrane was washed 3 times and probed with HRP-Protein A (Zymed) for 30 min. Finally, the membrane was washed 3 times and developed with ECL (Amersham). No expression  
10 was detected by Western blot. Similarly, no expression was detected by Western blot when the Ra12-P501S-F fusion was used for expression in BL21CodonPlus by CE6 phage (Invitrogen).

An N-terminal fragment of P501S (amino acids 36-325 of SEQ ID NO: 113) was cloned down-stream of the first 30 amino acids of the *M. tuberculosis* antigen  
15 Ra12 in pET17b as follows. P501S DNA was used to perform PCR using the primers AW025 (SEQ ID NO: 485) and AW027 (SEQ ID NO: 487). AW027 is an antisense cloning primer that contains an EcoRI site and a stop codon. DNA amplification was performed essentially as described above. The resulting PCR product was cloned to Ra12 in pET17b at the HindIII and EcoRI sites. The fusion construct (referred to as  
20 Ra12-P501S-N) was confirmed by DNA sequencing.

The Ra12-P501S-N fusion construct was used for expression in BL21(DE3)pLysE, pLysS and CodonPlus, essentially as described above. Using Western blot analysis, protein bands were observed at the expected molecular weight of 36 kDa. Some high molecular weight bands were also observed, probably due to  
25 aggregation of the recombinant protein. No expression was detected by Western blot when the Ra12-P501S-F fusion was used for expression in BL21CodonPlus by CE6 phage.

A fusion construct comprising a C-terminal portion of P501S (amino acids 257-553 of SEQ ID NO: 113) located down-stream of the first 30 amino acids of  
30 the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 484) was prepared as follows. P501S

DNA was used to perform PCR using the primers AW026 (SEQ ID NO: 488) and AW003 (SEQ ID NO: 486). AW026 is a sense cloning primer that contains a HindIII site. DNA amplification was performed essentially as described above. The resulting PCR product was cloned to Ra12 in pET17b at the HindIII and EcoRI sites. The  
5 sequence for the fusion construct (referred to as Ra12-P501S-C) was confirmed.

The Ra12-P501S-C fusion construct was used for expression in BL21(DE3)pLysE, pLysS and CodonPlus, as described above. A small amount of protein was detected by Western blot, with some molecular weight aggregates also being observed. Expression was also detected by Western blot when the Ra12-P501S-C  
10 fusion was used for expression in BL21CodonPlus induced by CE6 phage.

A fusion construct comprising a fragment of P501S (amino acids 36-298 of SEQ ID NO: 113) located down-stream of the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 848) was prepared as follows. P501S DNA was used to perform PCR using the primers AW042 (SEQ ID NO: 849) and AW053 (SEQ ID NO: 850). AW042 is a sense  
15 cloning primer that contains a EcoRI site. AW053 is an antisense primer with stop and Xho I sites. DNA amplification was performed essentially as described above. The resulting PCR product was cloned to Ra12 in pET17b at the EcoRI and Xho I sites. The resulting fusion construct (referred to as Ra12-P501S-E2) was expressed in B834 (DE3) pLys S *E. coli* host cells in TB media for 2 h at room temperature. Expressed protein  
20 was purified by washing the inclusion bodies and running on a Ni-NTA column. The purified protein stayed soluble in buffer containing 20 mM Tris-HCl (pH 8), 100 mM NaCl, 10 mM  $\beta$ -Me and 5% glycerol. The determined cDNA and amino acid sequences for the expressed fusion protein are provided in SEQ ID NO: 851 and 852, respectfully.

25 b) Expression of P501S in Baculovirus

The Bac-to-Bac baculovirus expression system (BRL Life Technologies, Inc.) was used to express P501S protein in insect cells. Full-length P501S (SEQ ID NO: 113) was amplified by PCR and cloned into the XbaI site of the donor plasmid pFastBacI. The recombinant bacmid and baculovirus were prepared according to the

manufacturer's instructions. The recombinant baculovirus was amplified in Sf9 cells and the high titer viral stocks were utilized to infect High Five cells (Invitrogen) to make the recombinant protein. The identity of the full-length protein was confirmed by N-terminal sequencing of the recombinant protein and by Western blot analysis (Figure 7). Specifically, 0.6 million High Five cells in 6-well plates were infected with either the unrelated control virus BV/ECD\_PD (lane 2), with recombinant baculovirus for P501S at different amounts or MOIs (lanes 4-8), or were uninfected (lane 3). Cell lysates were run on SDS-PAGE under reducing conditions and analyzed by Western blot with the anti-P501S monoclonal antibody P501S-10E3-G4D3 (prepared as described below). Lane 1 is the biotinylated protein molecular weight marker (BioLabs).

The localization of recombinant P501S in the insect cells was investigated as follows. The insect cells overexpressing P501S were fractionated into fractions of nucleus, mitochondria, membrane and cytosol. Equal amounts of protein from each fraction were analyzed by Western blot with a monoclonal antibody against P501S. Due to the scheme of fractionation, both nucleus and mitochondria fractions contain some plasma membrane components. However, the membrane fraction is basically free from mitochondria and nucleus. P501S was found to be present in all fractions that contain the membrane component, suggesting that P501S may be associated with plasma membrane of the insect cells expressing the recombinant protein.

#### c) Expression of P501S in mammalian cells

Full-length P501S (553 amino acids; SEQ ID NO: 113) was cloned into various mammalian expression vectors, including pCEP4 (Invitrogen), pVR1012 (Vical, San Diego, CA) and a modified form of the retroviral vector pBMN, referred to as pBIB. Transfection of P501S/pCEP4 and P501S/pVR1012 into HEK293 fibroblasts was carried out using the Fugene transfection reagent (Boehringer Mannheim). Briefly, 2 ul of Fugene reagent was diluted into 100 ul of serum-free media and incubated at room temperature for 5-10 min. This mixture was added to 1 ug of P501S plasmid DNA, mixed briefly and incubated for 30 minutes at room temperature. The

Fugene/DNA mixture was added to cells and incubated for 24-48 hours. Expression of recombinant P501S in transfected HEK293 fibroblasts was detected by means of Western blot employing a monoclonal antibody to P501S.

Transfection of p501S/pCEP4 into CHO-K cells (American Type Culture Collection, Rockville, MD) was carried out using GenePorter transfection reagent (Gene Therapy Systems, San Diego, CA). Briefly, 15 µl of GenePorter was diluted in 500 µl of serum-free media and incubated at room temperature for 10 min. The GenePorter/media mixture was added to 2 µg of plasmid DNA that was diluted in 500 µl of serum-free media, mixed briefly and incubated for 30 min at room temperature. CHO-K cells were rinsed in PBS to remove serum proteins, and the GenePorter/DNA mix was added and incubated for 5 hours. The transfected cells were then fed an equal volume of 2x media and incubated for 24-48 hours.

FACS analysis of P501S transiently infected CHO-K cells, demonstrated surface expression of P501S. Expression was detected using rabbit polyclonal antisera raised against a P501S peptide, as described below. Flow cytometric analysis was performed using a FaCScan (Becton Dickinson), and the data were analyzed using the Cell Quest program.

#### d) Expression of P703P in Baculovirus

The cDNA for full-length P703P-DE5 (SEQ ID NO: 326), together with several flanking restriction sites, was obtained by digesting the plasmid pCDNA703 with restriction endonucleases Xba I and Hind III. The resulting restriction fragment (approx. 800 base pairs) was ligated into the transfer plasmid pFastBacI which was digested with the same restriction enzymes. The sequence of the insert was confirmed by DNA sequencing. The recombinant transfer plasmid pFBP703 was used to make recombinant bacmid DNA and baculovirus using the Bac-To-Bac Baculovirus expression system (BRL Life Technologies). High Five cells were infected with the recombinant virus BVP703, as described above, to obtain recombinant P703P protein:



e) Expression of P788P in *E. Coli*

A truncated, N-terminal portion, of P788P (residues 1-644 of SEQ ID NO: 777; referred to as P788P-N) fused with a C-terminal 6xHis Tag was expressed in *E. coli* as follows. P788P cDNA was amplified using the primers AW080 and AW081 (SEQ ID NO: 815 and 816). AW080 is a sense cloning primer with an NdeI site. AW081 is an antisense cloning primer with a XhoI site. The PCR-amplified P788P, as well as the vector pCRX1, were digested with NdeI and XhoI. Vector and insert were ligated and transformed into NovaBlue cells. Colonies were randomly screened for insert and then sequenced. P788P-N clone #6 was confirmed to be identical to the designed construct. The expression construct P788P-N #6/pCRX1 was transformed into *E. coli* BL21 CodonPlus-RIL competent cells. After induction, most of the cells grew well, achieving OD600 of greater than 2.0 after 3 hr. Coomassie stained SDS-PAGE showed an over-expressed band at about 75 kD. Western blot analysis using a 6xHisTag antibody confirmed the band was P788P-N. The determined cDNA sequence for P788P-N is provided in SEQ ID NO: 817, with the corresponding amino acid sequence being provided in SEQ ID NO: 818.

f) Expression of P510S in *E. coli*

The P510S protein has 9 potential transmembrane domains and is predicted to be located at the plasma membrane. The C-terminal protein of this protein, as well as the predicted third extracellular domain of P510S were expressed in *E. coli* as follows.

The expression construct referred to as Ra12-P501S-C was designed to have a 6 HisTag at the N-terminal end, followed by the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 819) and then the C-terminal portion of P510S (amino residues 1176-1261 of SEQ ID NO: 538). Full-length P510S was used to amplify the P510S-C fragment by PCR using the primers AW056 and AW057 (SEQ ID NO: 820 and 821, respectively). AW056 is a sense cloning primer with an EcoRI site. AW057 is an antisense primer with stop and XhoI sites. The amplified P501S fragment and Ra12/pCRX1 were digested with EcoRI and XhoI and then purified. The insert and

vector were ligated together and transformed into NovaBlue. Colonies were randomly screened for insert and sequences. For protein expression, the expression construct was transformed into *E. coli* BL21 (DE3) CodonPlus-RIL competent cells. A mini-induction screen was performed to optimize the expression conditions. After induction  
5 the cells grew well, achieving OD 600 nm greater than 2.0 after 3 hours. Coomassie stain SDS-PAGE showed a highly over-expressed band at approx. 30 kD. Though this is higher than the expected molecular weight, western blot analysis was positive, showing this band to be the His tag-containing protein. The optimized culture conditions are as follows. Dilute overnight culture/daytime culture (LB + kanamycin +  
10 chloramphenicol) into 2xYT (with kanamycin and chloramphenicol) at a ratio of 25 ml culture to 1 liter 2xYT. Allow to grow at 37 °C until OD600 = 0.6. Take an aliquot out as T0 sample. Add 1 mM IPTG and allow to grow at 30 °C for 3 hours. Take out a T3 sample, spin down cells and store at -80 °C. The determined cDNA and amino acid sequences for the Ra12-P510S-C construct are provided in SEQ ID NO: 822 and 825,  
15 respectively.

The expression construct P510S-C was designed to have a 5' added start codon and a glycine (GGA) codon and then the P510S C terminal fragment followed by the in frame 6x histidine tag and stop codon from the pET28b vector. The cloning strategy is similar to that used for Ra12-P510S-C, except that the PCR primers  
20 employed were those shown in SEQ ID NO: 828 and 829, respectively and the NcoI/XhoI cut in pET28b was used. The primer of SEQ ID NO: 828 created a 5' NcoI site and added a start codon. The antisense primer of SEQ ID NO: 829 creates a XhoI site on P510S C terminal fragment. Clones were confirmed by sequencing. For protein expression, the expression construct was transformed into *E. coli* BL21 (DE3)  
25 CodonPlus-RIL competent cells. An OD600 of greater than 2.0 was obtained 30 hours after induction. Coomassie stained SDS-PAGE showed an over-expressed band at about 11 kD. Western blot analysis confirmed that the band was P510S-C, as did N-terminal protein sequencing. The optimized culture conditions are as follows: dilute overnight culture/daytime culture (LB + kanamycin + chloramphenicol) into 2x YT (+  
30 kanamycin and chloramphenicol) at a ratio of 25 mL culture to 1 liter 2x YT, and allow

to grow at 37 °C until an OD 600 of about 0.5 is reached. Take out an aliquot as T0 sample. Add 1 mM IPTG and allow to grow at 30 °C for 3 hours. Spin down the cells and store at -80 °C until purification. The determined cDNA and amino acid sequences for the P510S-C construct are shown in SEQ ID NO: 823 and 826, respectively.

5           The predicted third extracellular domain of P510S (P510S-E3; residues 328-676 of SEQ ID NO: 538) was expressed in *E. coli* as follows. The P510S fragment was amplified by PCR using the primers shown in SEQ ID NO: 830 and 831. The primer of SEQ ID NO: 830 is a sense primer with an NdeI site for use in ligating into pPDM. The primer of SEQ ID NO: 831 is an antisense primer with an added XhoI site  
10 for use in ligating into pPDM. The resulting fragment was cloned to pPDM at the NdeI and XhoI sites. Clones were confirmed by sequencing. For protein expression, the clone was transformed into *E. coli* BL21 (DE3) CodonPlus-RIL competent cells. After induction, an OD600 of greater than 2.0 was achieved after 3 hours. Coomassie stained SDS-PAGE showed an over-expressed band at about 39 kD, and N-terminal sequencing  
15 confirmed the N-terminal to be that of P510S-E3. Optimized culture conditions are as follows: dilute overnight culture/daytime culture (LB + kanamycin + chloramphenicol) into 2x YT (kanamycin and chloramphenicol) at a ratio of 25 ml culture to 1 liter 2x YT. Allow to grow at 37 °C until OD 600 equals 0.6. Take out an aliquot as T0 sample. Add 1 mM IPTG and allow to grow at 30 °C for 3 hours. Take out a T3  
20 sample, spin down the cells and store at -80 °C until purification. The determined cDNA and amino acid sequences for the P510S-E3 construct are provided in SEQ ID NO: 824 and 827, respectively.

g) Expression of P775S in *E. Coli*

25           The antigen P775P contains multiple open reading frames (ORF). The third ORF, encoding the protein of SEQ ID NO: 483, has the best motif score. An expression fusion construct containing the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 819) and P775P-ORF3 with an N-terminal 6x HisTag was prepared as follows. P775P-ORF3 was amplified using the sense PCR primers of SEQ ID NO: 832 and the antisense PCR primer of SEQ ID NO: 833. The PCR amplified fragment of P775P and

Ra12/pCRX1 were digested with the restriction enzymes EcoRI and XhoI. Vector and insert were ligated and then transformed into NovaBlue cells. Colonies were randomly screened for insert and then sequenced. A clone having the desired sequence was transformed into *E. coli* BL21 (DE3) CodonPlus-RIL competent cells. Two hours after  
5 induction, the cell density peaked at OD600 of approximately 1.8. Coomassie stained SDS-PAGE showed an over-expressed band at about 31 kD. Western blot using 6x HisTag antibody confirmed that the band was Ra12-P775P-ORF3. The determined cDNA and amino acid sequences for the fusion construct are provided in SEQ ID NO: 834 and 835, respectively.

10

H) Expression of a P703P His tag fusion protein in *E. coli*

The cDNA for the coding region of P703P was prepared by PCR using the primers of SEQ ID NO: 836 and 837. The PCR product was digested with EcoRI restriction enzyme, gel purified and cloned into a modified pET28 vector with a His tag  
15 in frame, which had been digested with Eco72I and EcoRI restriction enzymes. The correct construct was confirmed by DNA sequence analysis and then transformed into *E. coli* BL21 (DE3) pLys S expression host cells. The determined amino acid and cDNA sequences for the expressed recombinant P703P are provided in SEQ ID NO: 838 and 839, respectively.

20

I) Expression of a P705P His tag fusion protein in *E. coli*

The cDNA for the coding region of P705P was prepared by PCR using the primers of SEQ ID NO: 840 and 841. The PCR product was digested with EcoRI restriction enzyme, gel purified and cloned into a modified pET28 vector with a His tag  
25 in frame, which had been digested with Eco72I and EcoRI restriction enzymes. The correct construct was confirmed by DNA sequence analysis and then transformed into *E. coli* BL21 (DE3) pLys S and BL21 (DE3) CodonPlus expression host cells. The determined amino acid and cDNA sequences for the expressed recombinant P705P are provided in SEQ ID NO: 842 and 843, respectively.

30

J) Expression of a P711P His tag fusion protein in *E. coli*

The cDNA for the coding region of P711P was prepared by PCR using the primers of SEQ ID NO: 844 and 845. The PCR product was digested with EcoRI restriction enzyme, gel purified and cloned into a modified pET28 vector with a His tag in frame, which had been digested with Eco72I and EcoRI restriction enzymes. The correct construct was confirmed by DNA sequence analysis and then transformed into *E. coli* BL21 (DE3) pLys S and BL21 (DE3) CodonPlus expression host cells. The determined amino acid and cDNA sequences for the expressed recombinant P711P are provided in SEQ ID NO: 846 and 847, respectively.

K) Expression of P767P in *E. coli*

The full-length coding region of P767P (amino acids 2-374 of SEQ ID NO: 590) was amplified by PCR using the primers PDM-468 and PDM-469 (SEQ ID NO: 935 and 936, respectively). DNA amplification was performed using 10 µl 10X Pfu buffer, 1 µl 10 mM dNTPs, 2 µl each of the PCR primers at 10 µM concentration, 83 µl water, 1.5 µl Pfu DNA polymerase (Stratagene, La Jolla, CA) and 1 µl DNA at 100 ng/µl. Denaturation at 96°C was performed for 2 min, followed by 40 cycles of 96°C for 20 sec, 66°C for 15 sec and by 72°C for 2 min., and lastly by 1 cycle of 72°C for 4 min. The PCR product was digested with XhoI and cloned into a modified pET28 vector with a histidine tag in frame on the 5' end that was digested with Eco72I and XhoI. The construct was confirmed to be correct through sequence analysis and transformed into *E. coli* BL21 pLysS and BL21 CodonPlus RP cells. The cDNA coding region for the recombinant B767P protein is provided in SEQ ID NO: 938, with the corresponding amino acid sequence being provided in SEQ ID NO: 941. The full-length P767P did not express at high enough levels for detection or purification.

A truncated coding region of P767P (referred to as B767P-B; amino acids 47-374 of SEQ ID NO: 590) was amplified by PCR using the primers PDM-573 and PDM-469 (SEQ ID NO: 937 and 936, respectively) and the PCR conditions described above for full-length P767P. The PCR product was digested with XhoI and cloned into the modified pET28 vector that was digested with Eco72I and XhoI. The

construct was confirmed to be correct through sequence analysis and transformed into *E. coli* BL21 pLysS and BL21 CodonPlus RP cells. The protein was found to be expressed in the inclusion body pellet. The coding region for the expressed B767P-B protein is provided in SEQ ID NO: 939, with the corresponding amino acid sequence  
5 being provided in SEQ ID NO: 940.

## EXAMPLE 18

### PREPARATION AND CHARACTERIZATION OF ANTIBODIES AGAINST PROSTATE-SPECIFIC POLYPEPTIDES

10

#### a) Preparation and Characterization of Polyclonal Antibodies against P703P, P504S and P509S

Polyclonal antibodies against P703P, P504S and P509S were prepared as follows.

15 Each prostate tumor antigen expressed in an *E. coli* recombinant expression system was grown overnight in LB broth with the appropriate antibiotics at 37°C in a shaking incubator. The next morning, 10 ml of the overnight culture was added to 500 ml of 2x YT plus appropriate antibiotics in a 2L-baffled Erlenmeyer flask. When the Optical Density (at 560 nm) of the culture reached 0.4-0.6, the cells were  
20 induced with IPTG (1 mM). Four hours after induction with IPTG, the cells were harvested by centrifugation. The cells were then washed with phosphate buffered saline and centrifuged again. The supernatant was discarded and the cells were either frozen for future use or immediately processed. Twenty ml of lysis buffer was added to the cell pellets and vortexed. To break open the *E. coli* cells, this mixture was then run  
25 through the French Press at a pressure of 16,000 psi. The cells were then centrifuged again and the supernatant and pellet were checked by SDS-PAGE for the partitioning of the recombinant protein. For proteins that localized to the cell pellet, the pellet was resuspended in 10 mM Tris pH 8.0, 1% CHAPS and the inclusion body pellet was washed and centrifuged again. This procedure was repeated twice more. The washed

inclusion body pellet was solubilized with either 8 M urea or 6 M guanidine HCl containing 10 mM Tris pH 8.0 plus 10 mM imidazole. The solubilized protein was added to 5 ml of nickel-chelate resin (Qiagen) and incubated for 45 min to 1 hour at room temperature with continuous agitation. After incubation, the resin and protein mixture were poured through a disposable column and the flow through was collected. The column was then washed with 10-20 column volumes of the solubilization buffer. The antigen was then eluted from the column using 8M urea, 10 mM Tris pH 8.0 and 300 mM imidazole and collected in 3 ml fractions. A SDS-PAGE gel was run to determine which fractions to pool for further purification.

As a final purification step, a strong anion exchange resin such as HiPrepQ (Biorad) was equilibrated with the appropriate buffer and the pooled fractions from above were loaded onto the column. Each antigen was eluted off the column with a increasing salt gradient. Fractions were collected as the column was run and another SDS-PAGE gel was run to determine which fractions from the column to pool. The pooled fractions were dialyzed against 10 mM Tris pH 8.0. The proteins were then vialled after filtration through a 0.22 micron filter and the antigens were frozen until needed for immunization.

Four hundred micrograms of each prostate antigen was combined with 100 micrograms of muramyl dipeptide (MDP). Every four weeks rabbits were boosted with 100 micrograms mixed with an equal volume of Incomplete Freund's Adjuvant (IFA). Seven days following each boost, the animal was bled. Sera was generated by incubating the blood at 4°C for 12-4 hours followed by centrifugation.

Ninety-six well plates were coated with antigen by incubating with 50 microliters (typically 1 microgram) of recombinant protein at 4 °C for 20 hours. 250 microliters of BSA blocking buffer was added to the wells and incubated at room temperature for 2 hours. Plates were washed 6 times with PBS/0.01% Tween. Rabbit sera was diluted in PBS. Fifty microliters of diluted sera was added to each well and incubated at room temperature for 30 min. Plates were washed as described above before 50 microliters of goat anti-rabbit horse radish peroxidase (HRP) at a 1:10000 dilution was added and incubated at room temperature for 30 min. Plates were again

washed as described above and 100 microliters of TMB microwell peroxidase substrate was added to each well. Following a 15 min incubation in the dark at room temperature, the colorimetric reaction was stopped with 100 microliters of 1N H<sub>2</sub>SO<sub>4</sub> and read immediately at 450 nm. All polyclonal antibodies showed immunoreactivity to the appropriate antigen.

b) Preparation and Characterization of Antibodies against P501S

A murine monoclonal antibody directed against the carboxy-terminus of the prostate-specific antigen P501S was prepared as follows.

A truncated fragment of P501S (amino acids 355-526 of SEQ ID NO: 113) was generated and cloned into the pET28b vector (Novagen) and expressed in *E. coli* as a thioredoxin fusion protein with a histidine tag. The trx-P501S fusion protein was purified by nickel chromatography, digested with thrombin to remove the trx fragment and further purified by an acid precipitation procedure followed by reverse phase HPLC.

Mice were immunized with truncated P501S protein. Serum bleeds from mice that potentially contained anti-P501S polyclonal sera were tested for P501S-specific reactivity using ELISA assays with purified P501S and trx-P501S proteins. Serum bleeds that appeared to react specifically with P501S were then screened for P501S reactivity by Western analysis. Mice that contained a P501S-specific antibody component were sacrificed and spleen cells were used to generate anti-P501S antibody producing hybridomas using standard techniques. Hybridoma supernatants were tested for P501S-specific reactivity initially by ELISA, and subsequently by FACS analysis of reactivity with P501S transduced cells. Based on these results, a monoclonal hybridoma referred to as 10E3 was chosen for further subcloning. A number of subclones were generated, tested for specific reactivity to P501S using ELISA and typed for IgG isotype. The results of this analysis are shown below in Table V. Of the 16 subclones tested, the monoclonal antibody 10E3-G4-D3 was selected for further study.



Table V

Isotype analysis of murine anti-P501S monoclonal antibodies

Hybridoma clone	Isotype	Estimated [Ig] in supernatant ( $\mu\text{g/ml}$ )
4D11	IgG1	14.6
1G1	IgG1	0.6
4F6	IgG1	72
4H5	IgG1	13.8
4H5-E12	IgG1	10.7
4H5-EH2	IgG1	9.2
4H5-H2-A10	IgG1	10
4H5-H2-A3	IgG1	12.8
4H5-H2-A10-G6	IgG1	13.6
4H5-H2-B11	IgG1	12.3
10E3	IgG2a	3.4
10E3-D4	IgG2a	3.8
10E3-D4-G3	IgG2a	9.5
10E3-D4-G6	IgG2a	10.4
10E3-E7	IgG2a	6.5
8H12	IgG2a	0.6

5                   The specificity of 10E3-G4-D3 for P501S was examined by FACS analysis. Specifically, cells were fixed (2% formaldehyde, 10 minutes), permeabilized (0.1% saponin, 10 minutes) and stained with 10E3-G4-D3 at 0.5 – 1  $\mu\text{g/ml}$ , followed by incubation with a secondary, FITC-conjugated goat anti-mouse Ig antibody (Pharmingen, San Diego, CA). Cells were then analyzed for FITC fluorescence using

10 an Excalibur fluorescence activated cell sorter. For FACS analysis of transduced cells, B-LCL were retrovirally transduced with P501S. For analysis of infected cells, B-LCL were infected with a vaccinia vector that expresses P501S. To demonstrate specificity in these assays, B-LCL transduced with a different antigen (P703P) and uninfected B-LCL vectors were utilized. 10E3-G4-D3 was shown to bind with P501S-transduced B-

15 LCL and also with P501S-infected B-LCL, but not with either uninfected cells or P703P-transduced cells.

To determine whether the epitope recognized by 10E3-G4-D3 was found on the surface or in an intracellular compartment of cells, B-LCL were transduced with P501S or HLA-B8 as a control antigen and either fixed and permeabilized as described

above or directly stained with 10E3-G4-D3 and analyzed as above. Specific recognition of P501S by 10E3-G4-D3 was found to require permeabilization, suggesting that the epitope recognized by this antibody is intracellular.

The reactivity of 10E3-G4-D3 with the three prostate tumor cell lines Lncap, PC-3 and DU-145, which are known to express high, medium and very low levels of P501S, respectively, was examined by permeabilizing the cells and treating them as described above. Higher reactivity of 10E3-G4-D3 was seen with Lncap than with PC-3, which in turn showed higher reactivity than DU-145. These results are in agreement with the real time PCR and demonstrate that the antibody specifically recognizes P501S in these tumor cell lines and that the epitope recognized in prostate tumor cell lines is also intracellular.

Specificity of 10E3-G4-D3 for P501S was also demonstrated by Western blot analysis. Lysates from the prostate tumor cell lines Lncap, DU-145 and PC-3, from P501S-transiently transfected HEK293 cells, and from non-transfected HEK293 cells were generated. Western blot analysis of these lysates with 10E3-G4-D3 revealed a 46 kDa immunoreactive band in Lncap, PC-3 and P501S-transfected HEK cells, but not in DU-145 cells or non-transfected HEK293 cells. P501S mRNA expression is consistent with these results since semi-quantitative PCR analysis revealed that P501S mRNA is expressed in Lncap, to a lesser but detectable level in PC-3 and not at all in DU-145 cells. Bacterially expressed and purified recombinant P501S (referred to as P501SStr2) was recognized by 10E3-G4-D3 (24 kDa), as was full-length P501S that was transiently expressed in HEK293 cells using either the expression vector VR1012 or pCEP4. Although the predicted molecular weight of P501S is 60.5 kDa, both transfected and "native" P501S run at a slightly lower mobility due to its hydrophobic nature.

Immunohistochemical analysis was performed on prostate tumor and a panel of normal tissue sections (prostate, adrenal, breast, cervix, colon, duodenum, gall bladder, ileum, kidney, ovary, pancreas, parotid gland, skeletal muscle, spleen and testis). Tissue samples were fixed in formalin solution for 24 hours and embedded in paraffin before being sliced into 10 micron sections. Tissue sections were permeabilized and incubated with 10E3-G4-D3 antibody for 1 hr. HRP-labeled anti-

mouse followed by incubation with DAB chromogen was used to visualize P501S immunoreactivity. P501S was found to be highly expressed in both normal prostate and prostate tumor tissue but was not detected in any of the other tissues tested.

To identify the epitope recognized by 10E3-G4-D3, an epitope mapping  
5 approach was pursued. A series of 13 overlapping 20-21 mers (5 amino acid overlap; SEQ ID NO: 489-501) was synthesized that spanned the fragment of P501S used to generate 10E3-G4-D3. Flat bottom 96 well microtiter plates were coated with either the peptides or the P501S fragment used to immunize mice, at 1 microgram/ml for 2 hours at 37 °C. Wells were then aspirated and blocked with phosphate buffered saline  
10 containing 1% (w/v) BSA for 2 hours at room temperature, and subsequently washed in PBS containing 0.1% Tween 20 (PBST). Purified antibody 10E3-G4-D3 was added at 2 fold dilutions (1000 ng – 16 ng) in PBST and incubated for 30 minutes at room temperature. This was followed by washing 6 times with PBST and subsequently incubating with HRP-conjugated donkey anti-mouse IgG (H+L) Affinipure F(ab')  
15 fragment (Jackson ImmunoResearch, West Grove, PA) at 1:20000 for 30 minutes. Plates were then washed and incubated for 15 minutes in tetramethyl benzidine. Reactions were stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using an ELISA plate reader. As shown in Fig. 8, reactivity was seen with the peptide of SEQ ID NO: 496 (corresponding to amino acids 439-459 of P501S) and with  
20 the P501S fragment but not with the remaining peptides, demonstrating that the epitope recognized by 10E3-G4-D3 is localized to amino acids 439-459 of SEQ ID NO: 113.

In order to further evaluate the tissue specificity of P501S, multi-array immunohistochemical analysis was performed on approximately 4700 different human tissues encompassing all the major normal organs as well as neoplasias derived from  
25 these tissues. Sixty-five of these human tissue samples were of prostate origin. Tissue sections 0.6 mm in diameter were formalin-fixed and paraffin embedded. Samples were pretreated with HIER using 10 mM citrate buffer pH 6.0 and boiling for 10 min. Sections were stained with 10E3-G4-D3 and P501S immunoreactivity was visualized with HRP. All the 65 prostate tissues samples (5 normal, 55 untreated prostate tumors,

5 hormone refractory prostate tumors) were positive, showing distinct perinuclear staining. All other tissues examined were negative for P501S expression.

c) Preparation and Characterization of Antibodies against P503S

5 A fragment of P503S (amino acids 113-241 of SEQ ID NO: 114) was expressed and purified from bacteria essentially as described above for P501S and used to immunize both rabbits and mice. Mouse monoclonal antibodies were isolated using standard hybridoma technology as described above. Rabbit monoclonal antibodies were isolated using Selected Lymphocyte Antibody Method (SLAM) technology at  
10 Immgenics Pharmaceuticals (Vancouver, BC, Canada). Table VI, below, lists the monoclonal antibodies that were developed against P503S.

Table VI

Antibody	Species
20D4	Rabbit
JA1	Rabbit
1A4	Mouse
1C3	Mouse
1C9	Mouse
1D12	Mouse
2A11	Mouse
2H9	Mouse
4H7	Mouse
8A8	Mouse
8D10	Mouse
9C12	Mouse
6D12	Mouse

15

The DNA sequences encoding the complementarity determining regions (CDRs) for the rabbit monoclonal antibodies 20D4 and JA1 were determined and are provided in SEQ ID NO: 502 and 503, respectively.

In order to better define the epitope binding region of each of the antibodies, a series of overlapping peptides were generated that span amino acids 109-213 of SEQ ID NO: 114. These peptides were used to epitope map the anti-P503S monoclonal antibodies by ELISA as follows. The recombinant fragment of P503S that was employed as the immunogen was used as a positive control. Ninety-six well microtiter plates were coated with either peptide or recombinant antigen at 20 ng/well overnight at 4 °C. Plates were aspirated and blocked with phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature then washed in PBS containing 0.1% Tween 20 (PBST). Purified rabbit monoclonal antibodies diluted in PBST were added to the wells and incubated for 30 min at room temperature. This was followed by washing 6 times with PBST and incubation with Protein-A HRP conjugate at a 1:2000 dilution for a further 30 min. Plates were washed six times in PBST and incubated with tetramethylbenzidine (TMB) substrate for a further 15 min. The reaction was stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using at ELISA plate reader. ELISA with the mouse monoclonal antibodies was performed with supernatants from tissue culture run neat in the assay.

All of the antibodies bound to the recombinant P503S fragment, with the exception of the negative control SP2 supernatant. 20D4, JA1 and 1D12 bound strictly to peptide #2101 (SEQ ID NO: 504), which corresponds to amino acids 151-169 of SEQ ID NO: 114. 1C3 bound to peptide #2102 (SEQ ID NO: 505), which corresponds to amino acids 165-184 of SEQ ID NO: 114. 9C12 bound to peptide #2099 (SEQ ID NO: 522), which corresponds to amino acids 120-139 of SEQ ID NO: 114. The other antibodies bind to regions that were not examined in these studies.

Subsequent to epitope mapping, the antibodies were tested by FACS analysis on a cell line that stably expressed P503S to confirm that the antibodies bind to cell surface epitopes. Cells stably transfected with a control plasmid were employed as a negative control. Cells were stained live with no fixative. 0.5 ug of anti-P503S monoclonal antibody was added and cells were incubated on ice for 30 min before being washed twice and incubated with a FITC-labelled goat anti-rabbit or mouse secondary antibody for 20 min. After being washed twice, cells were analyzed with an Excalibur

fluorescent activated cell sorter. The monoclonal antibodies 1C3, 1D12, 9C12, 20D4 and JA1, but not 8D3, were found to bind to a cell surface epitope of P503S.

In order to determine which tissues express P503S, immunohistochemical analysis was performed, essentially as described above, on a panel of normal tissues (prostate, adrenal, breast, cervix, colon, duodenum, gall bladder, ileum, kidney, ovary, pancreas, parotid gland, skeletal muscle, spleen and testis). HRP-labeled anti-mouse or anti-rabbit antibody followed by incubation with TMB was used to visualize P503S immunoreactivity. P503S was found to be highly expressed in prostate tissue, with lower levels of expression being observed in cervix, colon, ileum and kidney, and no expression being observed in adrenal, breast, duodenum, gall bladder, ovary, pancreas, parotid gland, skeletal muscle, spleen and testis.

Western blot analysis was used to characterize anti-P503S monoclonal antibody specificity. SDS-PAGE was performed on recombinant (rec) P503S expressed in and purified from bacteria and on lysates from HEK293 cells transfected with full length P503S. Protein was transferred to nitrocellulose and then Western blotted with each of the anti-P503S monoclonal antibodies (20D4, JA1, 1D12, 6D12 and 9C12) at an antibody concentration of 1 ug/ml. Protein was detected using horse radish peroxidase (HRP) conjugated to either a goat anti-mouse monoclonal antibody or to protein A-sepharose. The monoclonal antibody 20D4 detected the appropriate molecular weight 14 kDa recombinant P503S (amino acids 113-241) and the 23.5 kDa species in the HEK293 cell lysates transfected with full length P503S. Other anti-P503S monoclonal antibodies displayed similar specificity by Western blot.

#### d) Preparation and Characterization of Antibodies against P703P

Rabbits were immunized with either a truncated (P703Ptr1; SEQ ID NO: 172) or full-length mature form (P703Pfl; SEQ ID NO: 523) of recombinant P703P protein was expressed in and purified from bacteria as described above. Affinity purified polyclonal antibody was generated using immunogen P703Pfl or P703Ptr1 attached to a solid support. Rabbit monoclonal antibodies were isolated using SLAM

technology at Immgenics Pharmaceuticals. Table VII below lists both the polyclonal and monoclonal antibodies that were generated against P703P.

Table VII

Antibody	Immunogen	Species/type
Aff. Purif. P703P (truncated); #2594	P703Ptrl	Rabbit polyclonal
Aff. Purif. P703P (full length); #9245	P703Pfl	Rabbit polyclonal
2D4	P703Ptrl	Rabbit monoclonal
8H2	P703Ptrl	Rabbit monoclonal
7H8	P703Ptrl	Rabbit monoclonal

The DNA sequences encoding the complementarity determining regions (CDRs) for the rabbit monoclonal antibodies 8H2, 7H8 and 2D4 were determined and are provided in SEQ ID NO: 506-508, respectively.

Epitope mapping studies were performed as described above. Monoclonal antibodies 2D4 and 7H8 were found to specifically bind to the peptides of SEQ ID NO: 509 (corresponding to amino acids 145-159 of SEQ ID NO: 172) and SEQ ID NO: 510 (corresponding to amino acids 11-25 of SEQ ID NO: 172), respectively. The polyclonal antibody 2594 was found to bind to the peptides of SEQ ID NO: 511-514, with the polyclonal antibody 9427 binding to the peptides of SEQ ID NO: 515-517.

The specificity of the anti-P703P antibodies was determined by Western blot analysis as follows. SDS-PAGE was performed on (1) bacterially expressed recombinant antigen; (2) lysates of HEK293 cells and Ltk<sup>-/-</sup> cells either untransfected or transfected with a plasmid expressing full length P703P; and (3) supernatant isolated from these cell cultures. Protein was transferred to nitrocellulose and then Western blotted using the anti-P703P polyclonal antibody #2594 at an antibody concentration of 1 ug/ml. Protein was detected using horse radish peroxidase (HRP) conjugated to an anti-rabbit antibody. A 35 kDa immunoreactive band could be observed with recombinant P703P. Recombinant P703P runs at a slightly higher molecular weight since it is epitope tagged. In lysates and supernatants from cells transfected with full length P703P, a 30 kDa band corresponding to P703P was observed. To assure

specificity, lysates from HEK293 cells stably transfected with a control plasmid were also tested and were negative for P703P expression. Other anti-P703P antibodies showed similar results.

Immunohistochemical studies were performed as described above, using anti-P703P monoclonal antibody. P703P was found to be expressed at high levels in normal prostate and prostate tumor tissue but was not detectable in all other tissues tested (breast tumor, lung tumor and normal kidney).

e) Preparation and Characterization of Antibodies against P504S

Full-length P504S (SEQ ID NO: 108) was expressed and purified from bacteria essentially as described above for P501S and employed to raise rabbit monoclonal antibodies using Selected Lymphocyte Antibody Method (SLAM) technology at Immgenics Pharmaceuticals (Vancouver, BC, Canada). The anti-P504S monoclonal antibody 13H4 was shown by Western blot to bind to both expressed recombinant P504S and to native P504S in tumor cells.

Immunohistochemical studies using 13H4 to assess P504S expression in various prostate tissues were performed as described above. A total of 104 cases, including 65 cases of radical prostatectomies with prostate cancer (PC), 26 cases of prostate biopsies and 13 cases of benign prostate hyperplasia (BPH), were stained with the anti-P504S monoclonal antibody 13H4. P504S showed strongly cytoplasmic granular staining in 64/65 (98.5%) of PCs in prostatectomies and 26/26 (100%) of PCs in prostatic biopsies. P504S was stained strongly and diffusely in carcinomas (4+ in 91.2% of cases of PC; 3+ in 5.5%; 2+ in 2.2% and 1+ in 1.1%) and high grade prostatic intraepithelial neoplasia (4+ in all cases). The expression of P504S did not vary with Gleason score. Only 17/91 (18.7%) of cases of NP/BPH around PC and 2/13 (15.4%) of BPH cases were focally (1+, no 2+ to 4+ in all cases) and weakly positive for P504S in large glands. Expression of P504S was not found in small atrophic glands, postatrophic hyperplasia, basal cell hyperplasia and transitional cell metaplasia in either biopsies or prostatectomies. P504S was thus found to be over-expressed in all Gleason scores of prostate cancer (98.5 to 100% of sensitivity) and exhibited only focal positivities in



large normal glands in 19/104 of cases (82.3% of specificity). These findings indicate that P504S may be usefully employed for the diagnosis of prostate cancer.

#### EXAMPLE 19

##### 5 CHARACTERIZATION OF CELL SURFACE EXPRESSION AND CHROMOSOME LOCALIZATION OF THE PROSTATE-SPECIFIC ANTIGEN P501S

This example describes studies demonstrating that the prostate-specific antigen P501S is expressed on the surface of cells, together with studies to determine  
10 the probable chromosomal location of P501S.

The protein P501S (SEQ ID NO: 113) is predicted to have 11 transmembrane domains. Based on the discovery that the epitope recognized by the anti-P501S monoclonal antibody 10E3-G4-D3 (described above in Example 17) is intracellular, it was predicted that following transmembrane determinants would allow  
15 the prediction of extracellular domains of P501S. Fig. 9 is a schematic representation of the P501S protein showing the predicted location of the transmembrane domains and the intracellular epitope described in Example 17. Underlined sequence represents the predicted transmembrane domains, bold sequence represents the predicted extracellular domains, and italicized sequence represents the predicted intracellular domains.  
20 Sequence that is both bold and underlined represents sequence employed to generate polyclonal rabbit serum. The location of the transmembrane domains was predicted using HHMTOP as described by Tusnady and Simon (Principles Governing Amino Acid Composition of Integral Membrane Proteins: Applications to Topology Prediction, *J. Mol. Biol.* 283:489-506, 1998).

25 Based on Fig. 9, the P501S domain flanked by the transmembrane domains corresponding to amino acids 274-295 and 323-342 is predicted to be extracellular. The peptide of SEQ ID NO: 518 corresponds to amino acids 306-320 of P501S and lies in the predicted extracellular domain. The peptide of SEQ ID NO: 519, which is identical to the peptide of SEQ ID NO: 518 with the exception of the  
30 substitution of the histidine with an asparagine, was synthesized as described above. A

Cys-Gly was added to the C-terminus of the peptide to facilitate conjugation to the carrier protein. Cleavage of the peptide from the solid support was carried out using the following cleavage mixture: trifluoroacetic acid:ethanediol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for two hours, the peptide was precipitated in cold ether.

- 5 The peptide pellet was then dissolved in 10% v/v acetic acid and lyophilized prior to purification by C18 reverse phase hplc. A gradient of 5-60% acetonitrile (containing 0.05% TFA) in water (containing 0.05% TFA) was used to elute the peptide. The purity of the peptide was verified by hplc and mass spectrometry, and was determined to be >95%. The purified peptide was used to generate rabbit polyclonal antisera as described  
10 above.

- Surface expression of P501S was examined by FACS analysis. Cells were stained with the polyclonal anti-P501S peptide serum at 10 µg/ml, washed, incubated with a secondary FITC-conjugated goat anti-rabbit Ig antibody (ICN), washed and analyzed for FITC fluorescence using an Excalibur fluorescence activated cell  
15 sorter. For FACS analysis of transduced cells, B-LCL were retrovirally transduced with P501S. To demonstrate specificity in these assays, B-LCL transduced with an irrelevant antigen (P703P) or nontransduced were stained in parallel. For FACS analysis of prostate tumor cell lines, Lncap, PC-3 and DU-145 were utilized. Prostate tumor cell lines were dissociated from tissue culture plates using cell dissociation medium and  
20 stained as above. All samples were treated with propidium iodide (PI) prior to FACS analysis, and data was obtained from PI-excluding (*i.e.*, intact and non-permeabilized) cells. The rabbit polyclonal serum generated against the peptide of SEQ ID NO: 519 was shown to specifically recognize the surface of cells transduced to express P501S, demonstrating that the epitope recognized by the polyclonal serum is extracellular.

- 25 To determine biochemically if P501S is expressed on the cell surface, peripheral membranes from Lncap cells were isolated and subjected to Western blot analysis. Specifically, Lncap cells were lysed using a dounce homogenizer in 5 ml of homogenization buffer (250 mM sucrose, 10 mM HEPES, 1mM EDTA, pH 8.0, 1 complete protease inhibitor tablet (Boehringer Mannheim)). Lysate samples were spun  
30 at 1000 g for 5 min at 4 °C. The supernatant was then spun at 8000g for 10 min at 4 °C.

Supernatant from the 8000g spin was recovered and subjected to a 100,000g spin for 30 min at 4 °C to recover peripheral membrane. Samples were then separated by SDS-PAGE and Western blotted with the mouse monoclonal antibody 10E3-G4-D3 (described above in Example 17) using conditions described above. Recombinant purified P501S, as well as HEK293 cells transfected with and over-expressing P501S were included as positive controls for P501S detection. LCL cell lysate was included as a negative control. P501S could be detected in Lncap total cell lysate, the 8000g (internal membrane) fraction and also in the 100,000g (plasma membrane) fraction. These results indicate that P501S is expressed at, and localizes to, the peripheral membrane.

To demonstrate that the rabbit polyclonal antiserum generated to the peptide of SEQ ID NO: 519 specifically recognizes this peptide as well as the corresponding native peptide of SEQ ID NO: 518, ELISA analyses were performed. For these analyses, flat-bottomed 96 well microtiter plates were coated with either the peptide of SEQ ID NO: 519, the longer peptide of SEQ ID NO: 520 that spans the entire predicted extracellular domain, the peptide of SEQ ID NO: 521 which represents the epitope recognized by the P501S-specific antibody 10E3-G4-D3, or a P501S fragment (corresponding to amino acids 355-526 of SEQ ID NO: 113) that does not include the immunizing peptide sequence, at 1 µg/ml for 2 hours at 37 °C. Wells were aspirated, blocked with phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature and subsequently washed in PBS containing 0.1% Tween 20 (PBST). Purified anti-P501S polyclonal rabbit serum was added at 2 fold dilutions (1000 ng - 125 ng) in PBST and incubated for 30 min at room temperature. This was followed by washing 6 times with PBST and incubating with HRP-conjugated goat anti-rabbit IgG (H+L) Affinipure F(ab') fragment at 1:20000 for 30 min. Plates were then washed and incubated for 15 min in tetramethyl benzidine. Reactions were stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using an ELISA plate reader. As shown in Fig. 11, the anti-P501S polyclonal rabbit serum specifically recognized the peptide of SEQ ID NO: 519 used in the immunization as well as the longer peptide of

SEQ ID NO: 520, but did not recognize the irrelevant P501S-derived peptides and fragments.

In further studies, rabbits were immunized with peptides derived from the P501S sequence and predicted to be either extracellular or intracellular, as shown in Fig. 9. Polyclonal rabbit sera were isolated and polyclonal antibodies in the serum were purified, as described above. To determine specific reactivity with P501S, FACS analysis was employed, utilizing either B-LCL transduced with P501S or the irrelevant antigen P703P, of B-LCL infected with vaccinia virus-expressing P501S. For surface expression, dead and non-intact cells were excluded from the analysis as described above. For intracellular staining, cells were fixed and permeabilized as described above. Rabbit polyclonal serum generated against the peptide of SEQ ID NO: 548, which corresponds to amino acids 181-198 of P501S, was found to recognize a surface epitope of P501S. Rabbit polyclonal serum generated against the peptide SEQ ID NO: 551, which corresponds to amino acids 543-553 of P501S, was found to recognize an epitope that was either potentially extracellular or intracellular since in different experiments intact or permeabilized cells were recognized by the polyclonal sera. Based on similar deductive reasoning, the sequences of SEQ ID NO: 541-547, 549 and 550, which correspond to amino acids 109-122, 539-553, 509-520, 37-54, 342-359, 295-323, 217-274, 143-160 and 75-88, respectively, of P501S, can be considered to be potential surface epitopes of P501S recognized by antibodies.

In further studies, mouse monoclonal antibodies were raised against amino acids 296 to 322 to P501S, which are predicted to be in an extracellular domain. A/J mice were immunized with P501S/adenovirus, followed by subsequent boosts with an *E. coli* recombinant protein, referred to as P501N, that contains amino acids 296 to 322 of P501S, and with peptide 296-322 (SEQ ID NO: 898) coupled with KLH. The mice were subsequently used for splenic B cell fusions to generate anti-peptide hybridomas. The resulting 3 clones, referred to as 4F4 (IgG1,kappa), 4G5 (IgG2a,kappa) and 9B9 (IgG1,kappa), were grown for antibody production. The 4G5 mAb was purified by passing the supernatant over a Protein A-sepharose column,

followed by antibody elution using 0.2M glycine, pH 2.3. Purified antibody was neutralized by the addition of 1M Tris, pH 8, and buffer exchanged into PBS.

For ELISA analysis, 96 well plates were coated with P501S peptide 296-322 (referred to as P501-long), an irrelevant P775 peptide, P501S-N, P501TR2, P501S-long-KLH, P501S peptide 306-319 (referred to as P501-short)-KLH, or the irrelevant peptide 2073-KLH, all at a concentration of 2 ug/ml and allowed to incubate for 60 minutes at 37 °C. After coating, plates were washed 5X with PBS + 0.1% Tween and then blocked with PBS, 0.5% BSA, 0.4% Tween20 for 2 hours at room temperature. Following the addition of supernatants or purified mAb, the plates were incubated for 60 minutes at room temperature. Plates were washed as above and donkey anti-mouse IgHRP-linked secondary antibody was added and incubated for 30 minutes at room temperature, followed by a final washing as above. TMB peroxidase substrate was added and incubated 15 minutes at room temperature in the dark. The reaction was stopped by the addition of 1N H<sub>2</sub>SO<sub>4</sub> and the OD was read at 450 nM. All three hybrid clones secreted mAb that recognized peptide 296-322 and the recombinant protein P501N.

For FACS analysis, HEK293 cells were transiently transfected with a P501S/VR1012 expression constructs using Fugene 6 reagent. After 2 days of culture, cells were harvested and washed, then incubated with purified 4G5 mAb for 30 minutes on ice. After several washes in PBS, 0.5% BSA, 0.01% azide, goat anti-mouse Ig-FITC was added to the cells and incubated for 30 minutes on ice. Cells were washed and resuspended in wash buffer including 1% propidium iodide and subjected to FACS analysis. The FACS analysis confirmed that amino acids 296-322 of P501S are in an extracellular domain and are cell surface expressed.

The chromosomal location of P501S was determined using the GeneBridge 4 Radiation Hybrid panel (Research Genetics). The PCR primers of SEQ ID NO: 528 and 529 were employed in PCR with DNA pools from the hybrid panel according to the manufacturer's directions. After 38 cycles of amplification, the reaction products were separated on a 1.2% agarose gel, and the results were analyzed through the Whitehead Institute/MIT Center for Genome Research web server

(<http://www-genome.wi.mit.edu/cgi-bin/contig/rhmapper.pl>) to determine the probable chromosomal location. Using this approach, P501S was mapped to the long arm of chromosome 1 at WI-9641 between q32 and q42. This region of chromosome 1 has been linked to prostate cancer susceptibility in hereditary prostate cancer (Smith *et al.* *Science* 274:1371-1374, 1996 and Berthon *et al.* *Am. J. Hum. Genet.* 62:1416-1424, 1998). These results suggest that P501S may play a role in prostate cancer malignancy.

## EXAMPLE 20

### REGULATION OF EXPRESSION OF THE PROSTATE-SPECIFIC ANTIGEN P501S

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Steroid (androgen) hormone modulation is a common treatment modality in prostate cancer. The expression of a number of prostate tissue-specific antigens have previously been demonstrated to respond to androgen. The responsiveness of the prostate-specific antigen P501S to androgen treatment was examined in a tissue culture system as follows.

15

Cells from the prostate tumor cell line LNCaP were plated at  $1.5 \times 10^6$  cells/T75 flask (for RNA isolation) or  $3 \times 10^5$  cells/well of a 6-well plate (for FACS analysis) and grown overnight in RPMI 1640 media containing 10% charcoal-stripped fetal calf serum (BRL Life Technologies, Gaithersburg, MD). Cell culture was continued for an additional 72 hours in RPMI 1640 media containing 10% charcoal-stripped fetal calf serum, with 1 nM of the synthetic androgen Methyltrienolone (R1881; New England Nuclear) added at various time points. Cells were then harvested for RNA isolation and FACS analysis at 0, 1, 2, 4, 8, 16, 24, 28 and 72-hours post androgen addition. FACS analysis was performed using the anti-P501S antibody 10E3-G4-D3 and permeabilized cells.

25

For Northern analysis, 5-10 micrograms of total RNA was run on a formaldehyde denaturing gel, transferred to Hybond-N nylon membrane (Amersham Pharmacia Biotech, Piscataway, NJ), cross-linked and stained with methylene blue. The filter was then prehybridized with Church's Buffer (250 mM  $\text{Na}_2\text{HPO}_4$ , 70 mM  $\text{H}_3\text{PO}_4$ , 1 mM EDTA, 1% SDS, 1% BSA in pH 7.2) at 65 °C for 1 hour. P501S DNA was

30

labeled with  $^{32}\text{P}$  using High Prime random-primed DNA labeling kit (Boehringer Mannheim). Unincorporated label was removed using MicroSpin S300-HR columns (Amersham Pharmacia Biotech). The RNA filter was then hybridized with fresh Church's Buffer containing labeled cDNA overnight, washed with 1X SCP (0.1 M NaCl, 0.03 M  $\text{Na}_2\text{HPO}_4 \cdot 7\text{H}_2\text{O}$ , 0.001 M  $\text{Na}_2\text{EDTA}$ ), 1% sarkosyl (n-lauroylsarcosine) and exposed to X-ray film.

Using both FACS and Northern analysis, P501S message and protein levels were found to increase in response to androgen treatment.

10

## EXAMPLE 21

## PREPARATION OF FUSION PROTEINS OF PROSTATE-SPECIFIC ANTIGENS

The example describes the preparation of a fusion protein of the prostate-specific antigen P703P and a truncated form of the known prostate antigen PSA. The truncated form of PSA has a 21 amino acid deletion around the active serine site. The expression construct for the fusion protein also has a restriction site at 3' end, immediately prior to the termination codon, to aid in adding cDNA for additional antigens.

The full-length cDNA for PSA was obtained by RT-PCR from a pool of RNA from human prostate tumor tissues using the primers of SEQ ID NO: 607 and 608, and cloned in the vector pCR-Blunt II-TOPO. The resulting cDNA was employed as a template to make two different fragments of PSA by PCR with two sets of primers (SEQ ID NO: 609 and 610; and SEQ ID NO: 611 and 612). The PCR products having the expected size were used as templates to make truncated forms of PSA by PCR with the primers of SEQ ID NO: 611 and 613, which generated PSA (delta 208-218 in amino acids). The cDNA for the mature form of P703P with a 6X histidine tag at the 5' end, was prepared by PCR with P703P and the primers of SEQ ID NO: 614 and 615. The cDNA for the fusion of P703P with the truncated form of PSA (referred to as FOPP) was then obtained by PCR using the modified P703P cDNA and the truncated form of PSA cDNA as templates and the primers of SEQ ID NO: 614 and 615. The FOPP

cDNA was cloned into the NdeI site and XhoI site of the expression vector pCRX1, and confirmed by DNA sequencing. The determined cDNA sequence for the fusion construct FOPP is provided in SEQ ID NO: 616, with the amino acid sequence being provided in SEQ ID NO: 617.

5                   The fusion FOPP was expressed as a single recombinant protein in *E. coli* as follows. The expression plasmid pCRX1FOPP was transformed into the *E. coli* strain BL21-CodonPlus RIL. The transformant was shown to express FOPP protein upon induction with 1 mM IPTG. The culture of the corresponding expression clone was inoculated into 25 ml LB broth containing 50 ug/ml kanamycin and 34 ug/ml  
10 chloramphenicol, grown at 37 °C to OD600 of about 1, and stored at 4 °C overnight. The culture was diluted into 1 liter of TB LB containing 50 ug/ml kanamycin and 34 ug/ml chloramphenicol, and grown at 37 °C to OD600 of 0.4. IPTG was added to a final concentration of 1 mM, and the culture was incubated at 30 °C for 3 hours. The cells were pelleted by centrifugation at 5,000 RPM for 8 min. To purify the protein, the  
15 cell pellet was suspended in 25 ml of 10 mM Tris-Cl pH 8.0, 2mM PMSF, complete protease inhibitor and 15 ug lysozyme. The cells were lysed at 4 °C for 30 minutes, sonicated several times and the lysate centrifuged for 30 minutes at 10,000 x g. The precipitate, which contained the inclusion body, was washed twice with 10 mM Tris-Cl pH 8.0 and 1% CHAPS. The inclusion body was dissolved in 40 ml of 10 mM Tris-Cl  
20 pH 8.0, 100 mM sodium phosphate and 8 M urea. The solution was bound to 8 ml Ni-NTA (Qiagen) for one hour at room temperature. The mixture was poured into a 25 ml column and washed with 50 ml of 10 mM Tris-Cl pH 6.3, 100 mM sodium phosphate, 0.5% DOC and 8M urea. The bound protein was eluted with 350 mM imidazole, 10 mM Tris-Cl pH 8.0, 100 mM sodium phosphate and 8 M urea. The fractions containing  
25 FOPP proteins were combined and dialyzed extensively against 10 mM Tris-Cl pH 4.6, aliquoted and stored at - 70 °C.



## EXAMPLE 22

REAL-TIME PCR CHARACTERIZATION OF THE PROSTATE-SPECIFIC ANTIGEN P501S IN  
PERIPHERAL BLOOD OF PROSTATE CANCER PATIENTS

5           Circulating epithelial cells were isolated from fresh blood of normal individuals and metastatic prostate cancer patients, mRNA isolated and cDNA prepared using real-time PCR procedures. Real-time PCR was performed with the Taqman<sup>TM</sup> procedure using both gene specific primers and probes to determine the levels of gene expression.

10           Epithelial cells were enriched from blood samples using an immunomagnetic bead separation method (Dynal A.S., Oslo, Norway). Isolated cells were lysed and the magnetic beads removed. The lysate was then processed for poly A+ mRNA isolation using magnetic beads coated with Oligo(dT)25. After washing the beads in buffer, bead/poly A+ RNA samples were suspended in 10 mM Tris HCl pH 8.0  
15 and subjected to reversed transcription. The resulting cDNA was subjected to real-time PCR using gene specific primers. Beta-actin content was also determined and used for normalization. Samples with P501S copies greater than the mean of the normal samples + 3 standard deviations were considered positive. Real time PCR on blood samples was performed using the Taqman<sup>TM</sup> procedure but extending to 50 cycles using  
20 forward and reverse primers and probes specific for P501S. Of the eight samples tested, 6 were positive for P501S and  $\beta$ -actin signal. The remaining 2 samples had no detectable  $\beta$ -actin or P501S. No P501S signal was observed in the four normal blood samples tested.

25

## EXAMPLE 23

EXPRESSION OF THE PROSTATE-SPECIFIC ANTIGENS P703P AND P501S IN  
SCID MOUSE-PASSAGED PROSTATE TUMORS

30           When considering the effectiveness of antigens in the treatment of prostate cancer, the continued presence of the antigens in tumors during androgen

ablation therapy is important. The presence of the prostate-specific antigens P703P and P501S in prostate tumor samples grown in SCID mice in the presence of testosterone was evaluated as follows.

Two prostate tumors that had metastasized to the bone were removed  
5 from patients, implanted into SCID mice and grown in the presence of testosterone. Tumors were evaluated for mRNA expression of P703P, P501S and PSA using quantitative real time PCR with the SYBR green assay method. Expression of P703P and P501S in a prostate tumor was used as a positive control and the absence in normal intestine and normal heart as negative controls. In both cases, the specific mRNA was  
10 present in late passage tumors. Since the bone metastases were grown in the presence of testosterone, this implies that the presence of these genes would not be lost during androgen ablation therapy.

#### EXAMPLE 24

##### 15 ANTI-P503S MONOCLONAL ANTIBODY INHIBITS TUMOR GROWTH *IN VIVO*

The ability of the anti-P503S monoclonal antibody 20D4 to suppress tumor formation in mice was examined as follows.

Ten SCID mice were injected subcutaneously with HEK293 cells that expressed P503S. Five mice received 150 micrograms of 20D4 intravenously at day 0  
20 (time of tumor cell injection), day 5 and day 9. Tumor size was measured for 50 days. Of the five animals that received no 20D4, three formed detectable tumors after about 2 weeks which continued to enlarge throughout the study. In contrast, none of the five mice that received 20D4 formed tumors. These results demonstrate that the anti-P503S Mab 20D4 displays potent anti-tumor activity *in vivo*.

25

#### EXAMPLE 25

##### CHARACTERIZATION OF A T CELL RECEPTOR CLONE FROM A P501S-SPECIFIC T CELL CLONE

30 T cells have a limited lifespan. However, cloning of T cell receptor (TCR) chains and subsequent transfer essentially enables infinite propagation of the T

cell specificity. Cloning of tumor-antigen TCR chains allows the transfer of the specificity into T cells isolated from patients that share the TCR MHC-restricting allele. Such T cells could then be expanded and used in adoptive transfer settings to introduce the tumor antigen specificity into patients carrying tumors that express the antigen. T cell receptor alpha and beta chains from a CD8 T cell clone specific for the prostate-specific antigen P501S were isolated and sequenced as follows.

Total mRNA from  $2 \times 10^6$  cells from CTL clone 4E5 (described above in Example 12) was isolated using Trizol reagent and cDNA was synthesized. To determine Va and Vb sequences in this clone, a panel of Va and Vb subtype-specific primers was synthesized and used in RT-PCR reactions with cDNA generated from each of the clones. The RT-PCR reactions demonstrated that each of the clones expressed a common Vb sequence that corresponded to the Vb7 subfamily. Furthermore, using cDNA generated from the clone, the Va sequence expressed was determined to be Va6. To clone the full TCR alpha and beta chains from clone 4E5, primers were designed that spanned the initiator and terminator-coding TCR nucleotides. The primers were as follows: TCR Valpha-6 5'(sense): GGATCC---GCCGCCACC---ATGTCACCTTTCTAGCCTGCT (SEQ ID NO: 899) BamHI site Kozak TCR alpha sequence TCR alpha 3' (antisense): GTCGAC---TCAGCTGGACCACAGCCGCAG (SEQ ID NO: 900) SalI site TCR alpha constant sequence TCR Vbeta-7. 5'(sense): GGATCC---GCCGCCACC--ATGGGCTGCAGGCTGCTCT (SEQ ID NO: 901) BamHI site Kozak TCR alpha sequence TCR beta 3' (antisense): GTCGAC---TCAGAAATCCTTTCTCTTGAC (SEQ ID NO: 902) SalI site TCR beta constant sequence. Standard 35 cycle RT-PCR reactions were established using cDNA synthesized from the CTL clone and the above primers, employing the proofreading thermostable polymerase PWO (Roche, Nutley, NJ).

The resultant specific bands (approx. 850 bp for alpha and approx. 950 for beta) were ligated into the PCR blunt vector (Invitrogen) and transformed into *E. coli*. *E. coli* transformed with plasmids containing full-length alpha and beta chains were identified, and large scale preparations of the corresponding plasmids were generated. Plasmids containing full-length TCR alpha and beta chains were submitted

for sequencing. The sequencing reactions demonstrated the cloning of full-length TCR alpha and beta chains with the determined cDNA sequences for the Vb and Va chains being shown in SEQ ID NO: 903 and 904, respectively. The corresponding amino acid sequences are shown in SEQ ID NO: 905 and 906, respectively. The Va sequence was shown by nucleotide sequence alignment to be 99% identical (347/348) to Va6.2, and the Vb to be 99% identical to Vb7 (336/338).

## EXAMPLE 26

### CAPTURE OF PROSTATE SPECIFIC CELLS USING

#### 10 THE PROSTATE ANTIGEN P503S

As described above, P503S is found on the surface of prostate cells. Secondary coated microsphere beads specific for mouse IgG were coupled with the purified P503S-specific monoclonal antibody 1D12. The bound P503S antibody was then used to capture HEK cells expressing recombinant P503S. This provides a model system for prostate-specific cell capture which may be usefully employed in the detection of prostate cells in blood, and therefore in the detection of prostate cancer.

P503S-transfected HEK cells were harvested and redissolved in wash buffer (PBS, 0.1% BSA, 0.6% sodium citrate) at an appropriate volume to give at least  $5^4$  cells per sample. Round bottom Eppendorf tubes were used for all procedures involving beads. The stock concentrations were as shown below in Table VIII.

Table VIII

Stock concentrations	Sample concentration	Amount needed
Epithelial enrich beads $4^8$ beads/ml (DynaI Biotech Inc. Lake Success, NY)	$1^7$ beads/ml	125 ul stock per 5 ml volume
1D12 ascites antibody 2 mg/ml	0.1 ug/ml (0.1X) to 5 ug/ml (5X) titrations	0.05 ul to 2.5 ul stock per sample
$\alpha$ - Mamma Mu 0.9 mg/ml	1 ug/ml (1X)	1.1 ul stock per sample
Pan-mouse IgG beads $4^8$ beads/ml (DynaI Biotech)	$1^7$ beads/ml	125 ul stock per 5 ml volume

Blocked immunomagnetic beads were pre-washed as follows: all beads needed were pooled and washed once with 1 ml wash buffer. The beads were resuspended in a 3X volume of 1% BSA (v/v) in wash buffer and incubated for 15 min rotating at 4 °C. The beads were then washed three times with 2X volume of wash  
5 buffer and resuspended to original volume. Non-blocked beads were pooled, washed three times with 2X volume of wash buffer and resuspended to original volume.

Primary antibody was incubated with secondary beads in a fresh Eppendorf for 30 minutes, rotating at 4 °C. Approximately 200 ul wash buffer was added to increase the total volume for even mixing of the sample. The antibody-bead  
10 solution was transferred to a fresh Eppendorf, washed twice with an equal volume of wash buffer and resuspended to original volume. Target cells were added to each sample and incubated for 45 minutes, rotating at 4 °C. The tubes were transferred to a magnet, the supernatant removed, taking care not to agitate the beads, and the samples were washed twice with 1 ml wash buffer. The samples were then ready for RT-PCR  
15 using a Dynabeads mRNA direct microkit (Dynal Biotech).

Epithelial cell enrichment was placed in a magnet and supernatant was removed. The epithelial enrichment beads were then resuspended in 100 ul lysis/binding buffer fortified with Rnasin (2 U/ul per sample), and stored at -70 °C until use. Oligo (dT<sub>25</sub>) Dynabeads were pre-washed as follows: all beads needed were pooled (23  
20 ul/sample), washed three times with an excess volume of lysis/binding buffer, and resuspended to original volume. The lysis supernatant was separated with a magnet and transferred to a fresh Eppendorf. 20 ul oligo(dT<sub>25</sub>) Dynabeads were added per sample and rolled for 5 min at room temperature. Supernatant was separated using a magnet and discarded, leaving the mRNA annealed to the beads. The bead/mRNA  
25 complex was washed with buffer and resuspended in cold Tris-HCl.

For RT-PCR, the Tris-HCl supernatant was separated and discarded using MPS. For each sample containing 1<sup>5</sup> cells or less, the following was added to give a total volume of 30 ul: 14.25 ul H<sub>2</sub>O; 1.5 ul BSA; 6 ul first strand buffer; 0.75 mL 10 mM dNTP mix; 3 ul Rnasin; 3 ul 0.1M dTT; and 1.5 ul Superscript II. The resulting  
30 solution was incubated for 1 hour at 42 °C, diluted 1:5 in H<sub>2</sub>O, heated at 80°C for 2 min

to detach cDNA from the beads, and immediately placed on MPS. The supernatant containing cDNA was transferred to a new tube and stored at  $-20^{\circ}\text{C}$ .

Table IX shows the percentage of capture of P503S-transfected HEK cells as determined by RT-PCR.

5

Table IX

	% capture P503S-transfected HEK cells	% capture LnCAP cells
0.1 ug/ml P503S Mab	36.90	0.00
0.5 ug/ml P503S Mab	67.40	2.93
1 ug/ml P503S Mab	40.22	0.00
5 ug/ml P503S Mab	13.11	0.00
Anti-Mu beads only, non-blocked	1.42	0.00
Anti-Mu beads only, blocked	15.65	20.21
Absolute control, non-capture cells	100.00	100.00

10

From the foregoing it will be appreciated that, although specific embodiments of the invention have been described herein for purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the invention is not limited except as by the appended claims.

## CLAIMS

## What is Claimed:

1. An isolated polynucleotide comprising a sequence selected from the group consisting of:

(a) sequences provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942;

(b) complements of the sequences provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942;

(c) sequences consisting of at least 20 contiguous residues of a sequence provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942;

(d) sequences that hybridize to a sequence provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942 under moderately stringent conditions;

(e) sequences having at least 75% identity to a sequence of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942;

(f) sequences having at least 90% identity to a sequence of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942; and

(g) degenerate variants of a sequence provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942.

2. An isolated polypeptide comprising an amino acid sequence selected from the group consisting of:

(a) sequences recited in SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586, 588-590, 592, 706-708, 775, 776, 778, 780, 781, 811, 814, 818, 826, 827, 853, 855, 858, 860-862, 866-877, 879, 883-893, 895, 897, 898, 909-915, 920-928, 932-934, 940, 941 and 943;

(b) sequences having at least 70% identity to a sequence of SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586, 588-590, 592, 706-708, 775, 776, 778, 780, 781, 811, 814, 818, 826, 827, 853, 855, 858, 860-862, 866-877, 879, 883-893, 895, 897, 898, 909-915, 920-928, 932-934, 940, 941 and 943;

(c) sequences having at least 90% identity to a sequence of SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586, 588-590, 592, 706-708, 775, 776, 778, 780, 781, 811, 814, 818, 826, 827, 853, 855, 858, 860-862, 866-877, 879, 883-893, 895, 897, 898, 909-915, 920-928, 932-934, 940, 941 and 943;

(d) sequences encoded by a polynucleotide of claim 1;



(e) sequences having at least 70% identity to a sequence encoded by a polynucleotide of claim 1; and

(f) sequences having at least 90% identity to a sequence encoded by a polynucleotide of claim 1.

3. An expression vector comprising a polynucleotide of claim 1 operably linked to an expression control sequence.

4. A host cell transformed or transfected with an expression vector according to claim 3.

5. An isolated antibody, or antigen-binding fragment thereof, that specifically binds to a polypeptide of claim 2.

6. A method for detecting the presence of a cancer in a patient, comprising the steps of:

(a) obtaining a biological sample from the patient;

(b) contacting the biological sample with a binding agent that binds to a polypeptide of claim 2;

(c) detecting in the sample an amount of polypeptide that binds to the binding agent; and

(d) comparing the amount of polypeptide to a predetermined cut-off value and therefrom determining the presence of a cancer in the patient.

7. A fusion protein comprising at least one polypeptide according to claim 2.

8. An oligonucleotide that hybridizes to a sequence recited in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591,

593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942 under moderately stringent conditions.

9. A method for stimulating and/or expanding T cells specific for a tumor protein, comprising contacting T cells with at least one component selected from the group consisting of:

- (a) polypeptides according to claim 2;
- (b) polynucleotides according to claim 1; and
- (c) antigen-presenting cells that express a polypeptide according to claim 2,

under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells.

10. An isolated T cell population, comprising T cells prepared according to the method of claim 9.

11. A composition comprising a first component selected from the group consisting of physiologically acceptable carriers and immunostimulants, and a second component selected from the group consisting of:

- (a) polypeptides according to claim 2;
- (b) polynucleotides according to claim 1;
- (c) antibodies according to claim 5;
- (d) fusion proteins according to claim 7;
- (e) T cell populations according to claim 10; and
- (f) antigen presenting cells that express a polypeptide according to claim 2.

12. A method for stimulating an immune response in a patient, comprising administering to the patient a composition of claim 11.

13. A method for the treatment of a cancer in a patient, comprising administering to the patient a composition of claim 11.

14. A method for determining the presence of a cancer in a patient, comprising the steps of:

- (a) obtaining a biological sample from the patient;
- (b) contacting the biological sample with an oligonucleotide according to claim 8;
- (c) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; and
- (d) compare the amount of polynucleotide that hybridizes to the oligonucleotide to a predetermined cut-off value, and therefrom determining the presence of the cancer in the patient.

15. A diagnostic kit comprising at least one oligonucleotide according to claim 8.

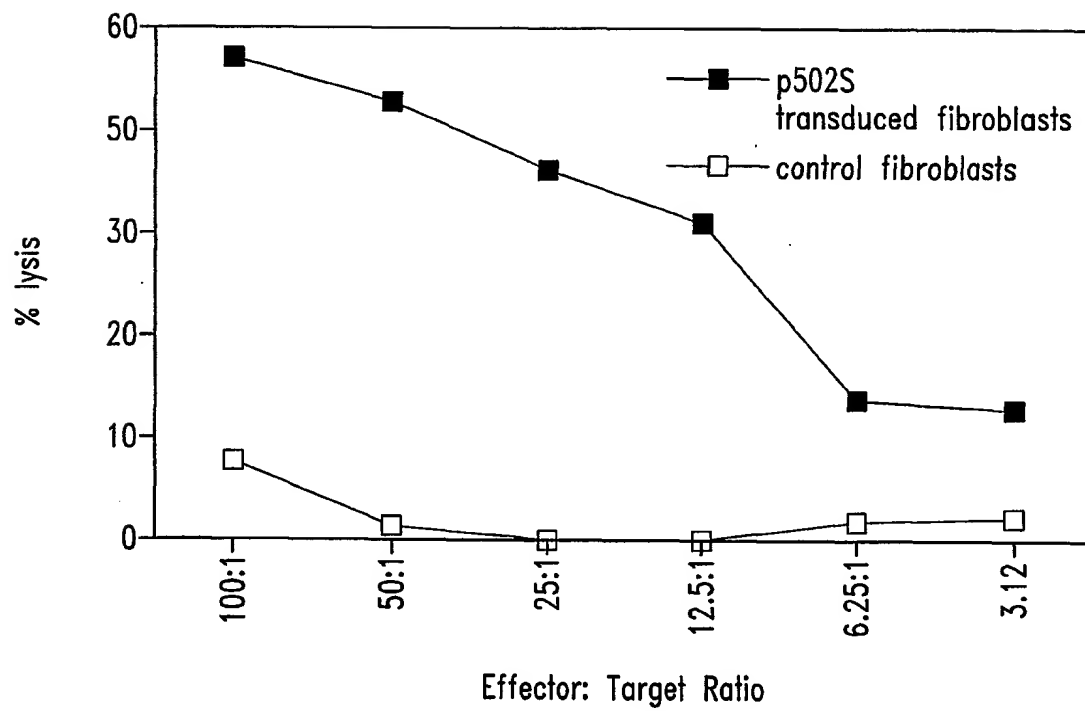
16. A diagnostic kit comprising at least one antibody according to claim 5 and a detection reagent, wherein the detection reagent comprises a reporter group.

17. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

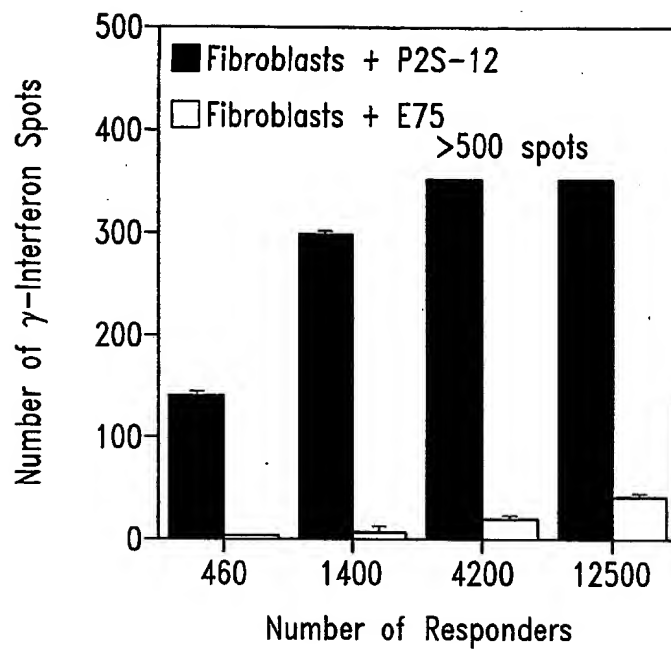
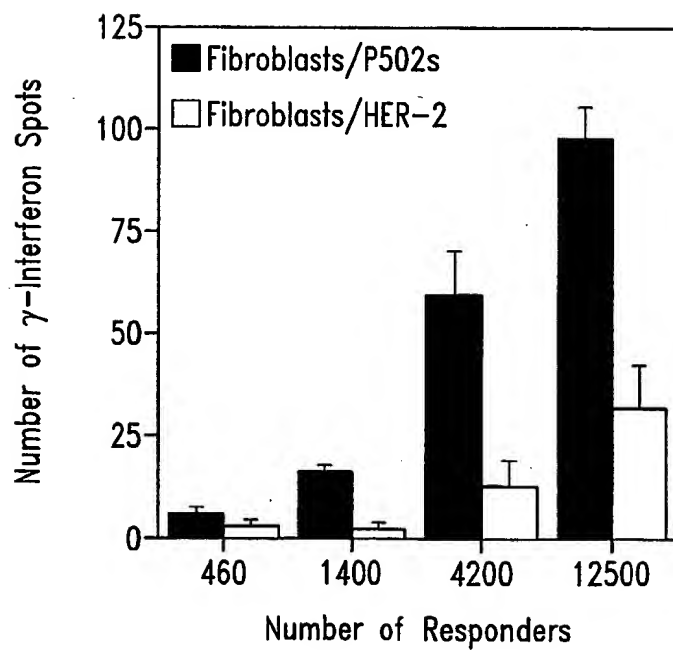
- (a) incubating CD4+ and/or CD8+ T cells isolated from a patient with at least one component selected from the group consisting of: (i) polypeptides according to claim 2; (ii) polynucleotides according to claim 1; and (iii) antigen presenting cells that express a polypeptide of claim 2, such that T cell proliferate;
- (b) administering to the patient an effective amount of the proliferated T cells,

and thereby inhibiting the development of a cancer in the patient.

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*Fig. 1*

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*Fig. 2A**Fig. 2B*

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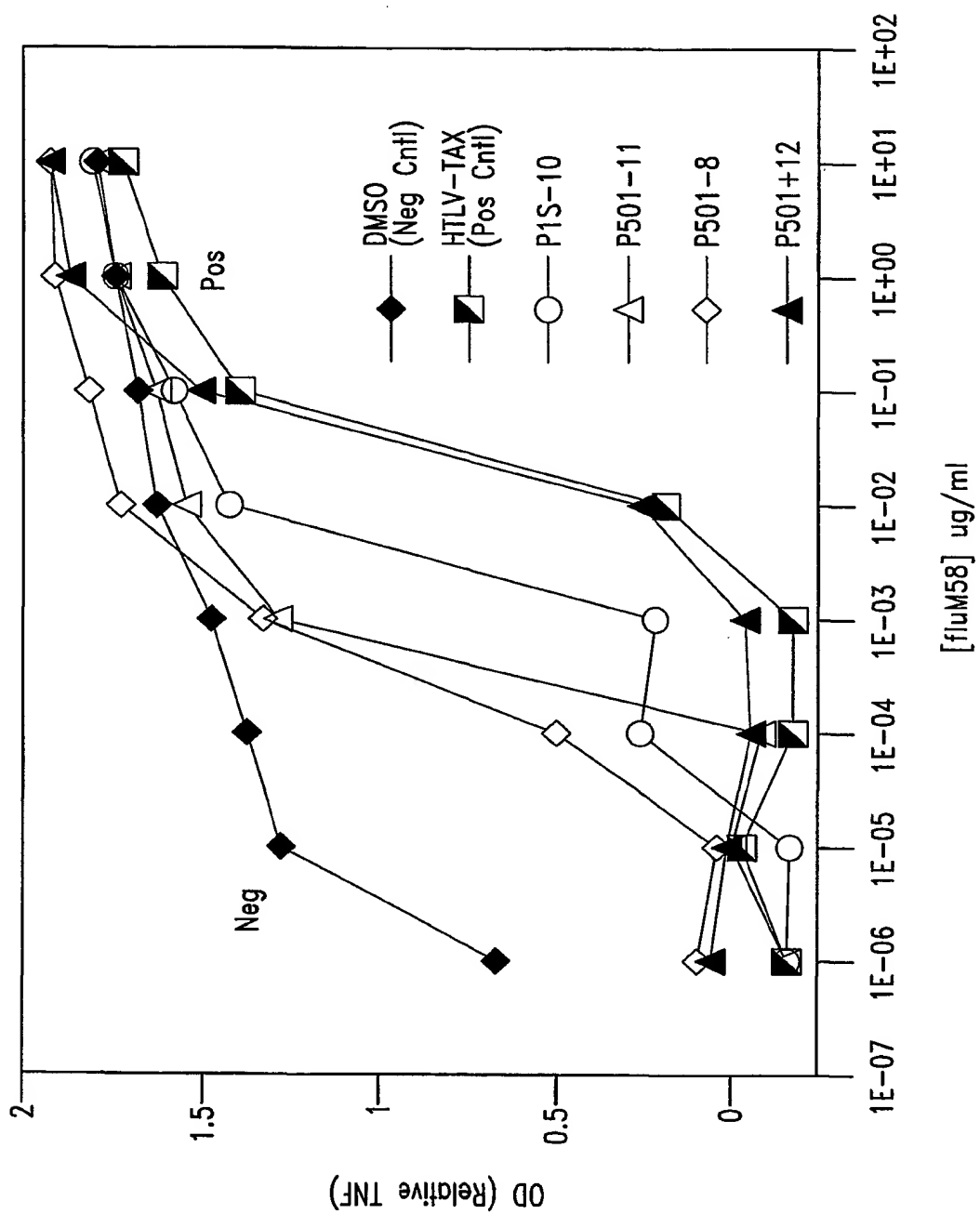
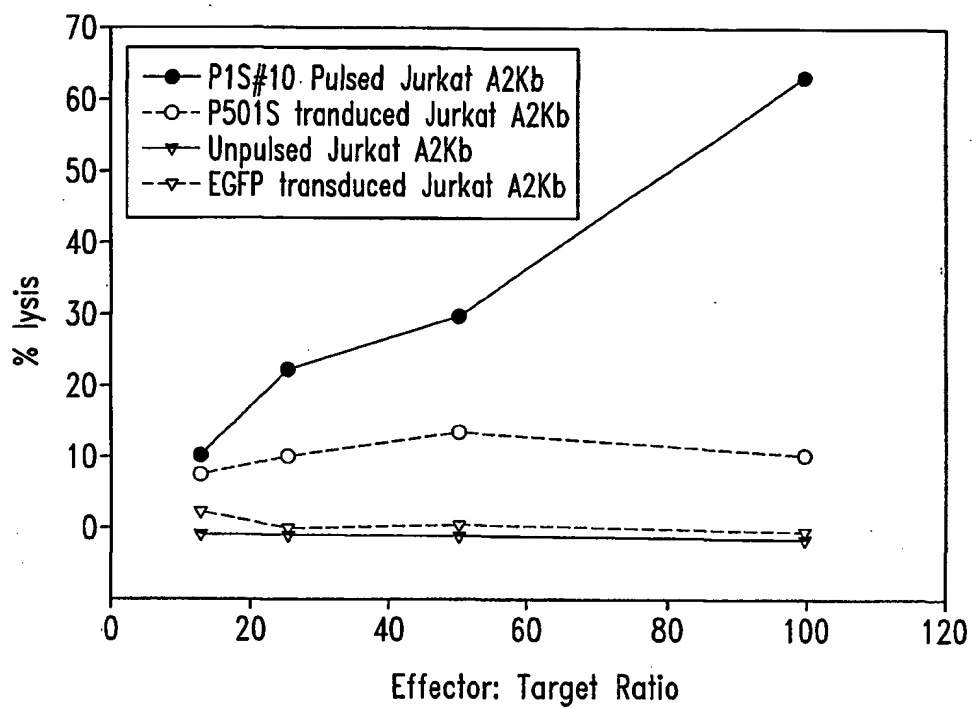
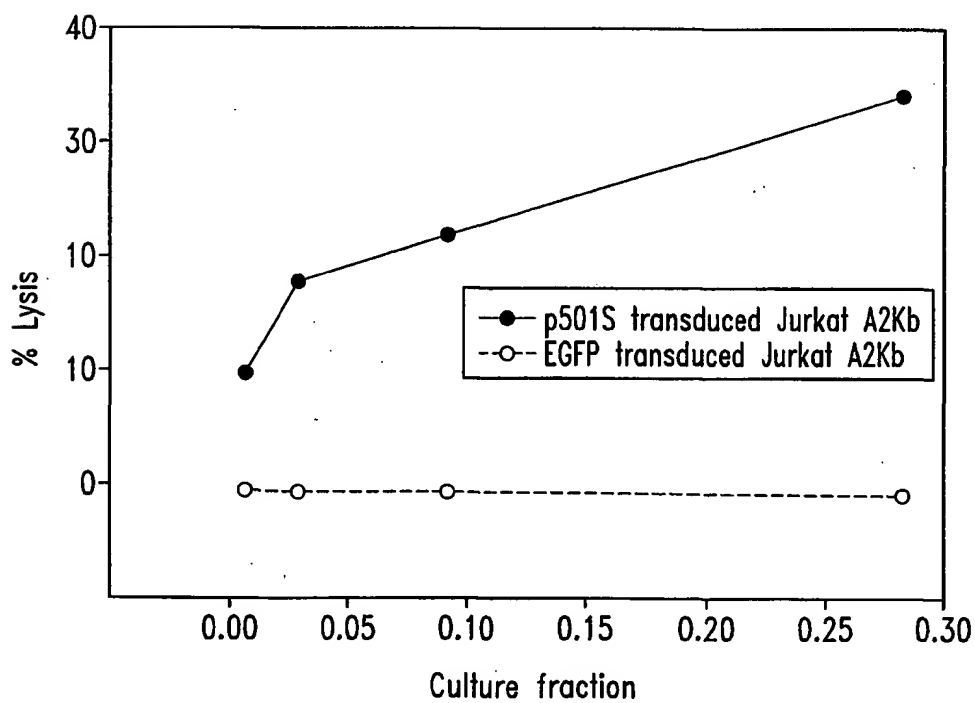
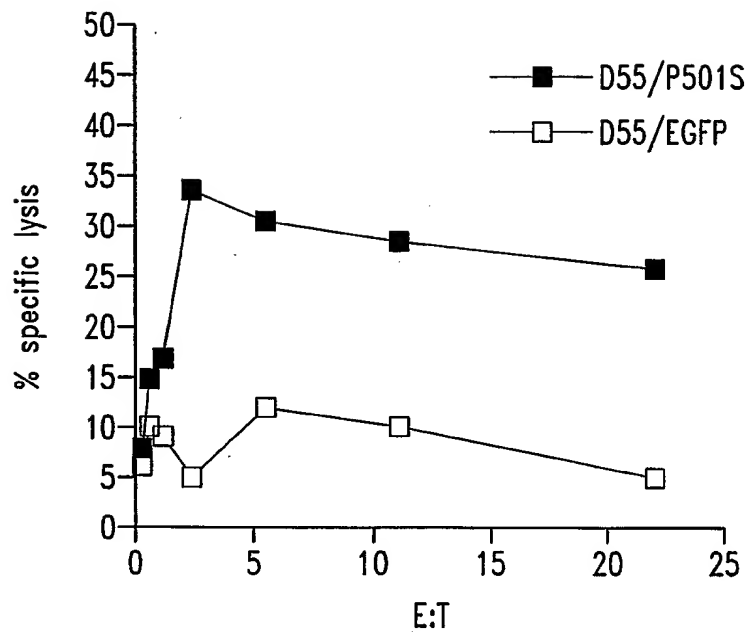
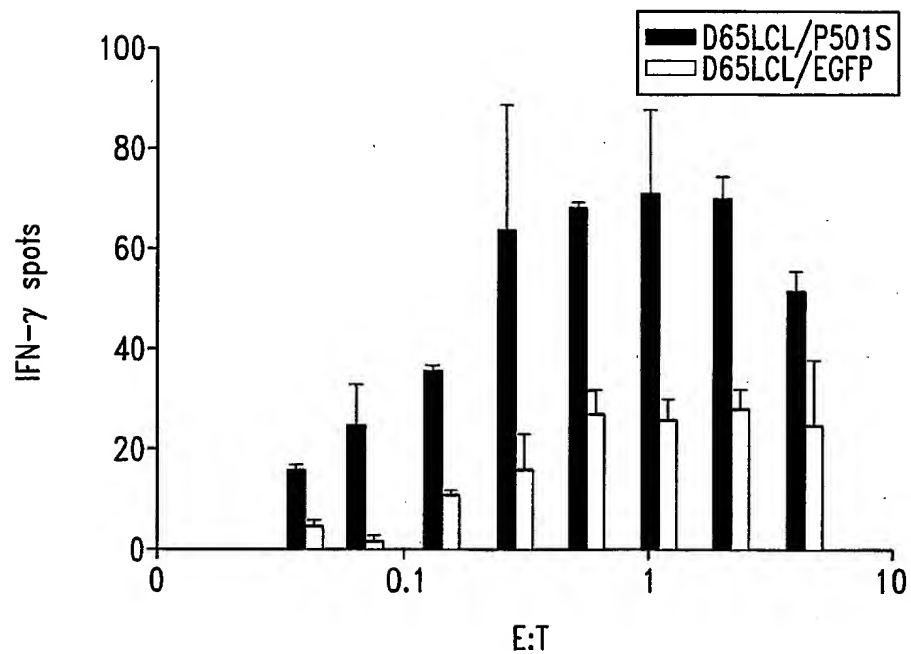


Fig. 3

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*Fig. 4**Fig. 5*

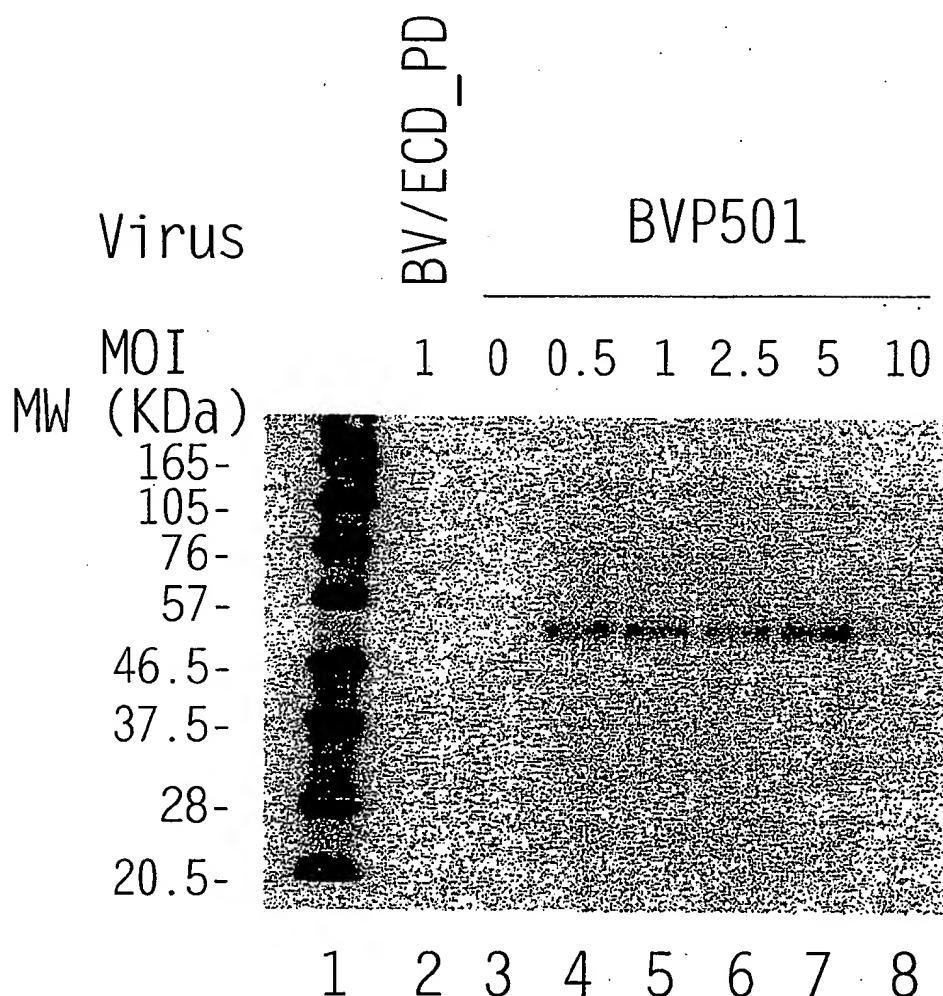
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*Fig. 6A**Fig. 6B*



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Expression of P501S  
by the Baculovirus Expression System



0.6 million high 5 cells in 6-well plate were infected with an unrelated control virus BV/ECD\_PD (lane2), without virus (lane3), or with recombinant baculovirus for P501 at different MOIs (lane 4-8). Cell lysates were run on SDS-PAGE under the reducing conditions and analyzed by Western blot with a monoclonal antibody against P501S (P501S-10E3-G4D3). Lane 1 is the biotinylated protein molecular weight marker (BioLabs).

*Fig. 7*

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FIGURE 8. Mapping of the epitope recognized by 10E3-G4-D3

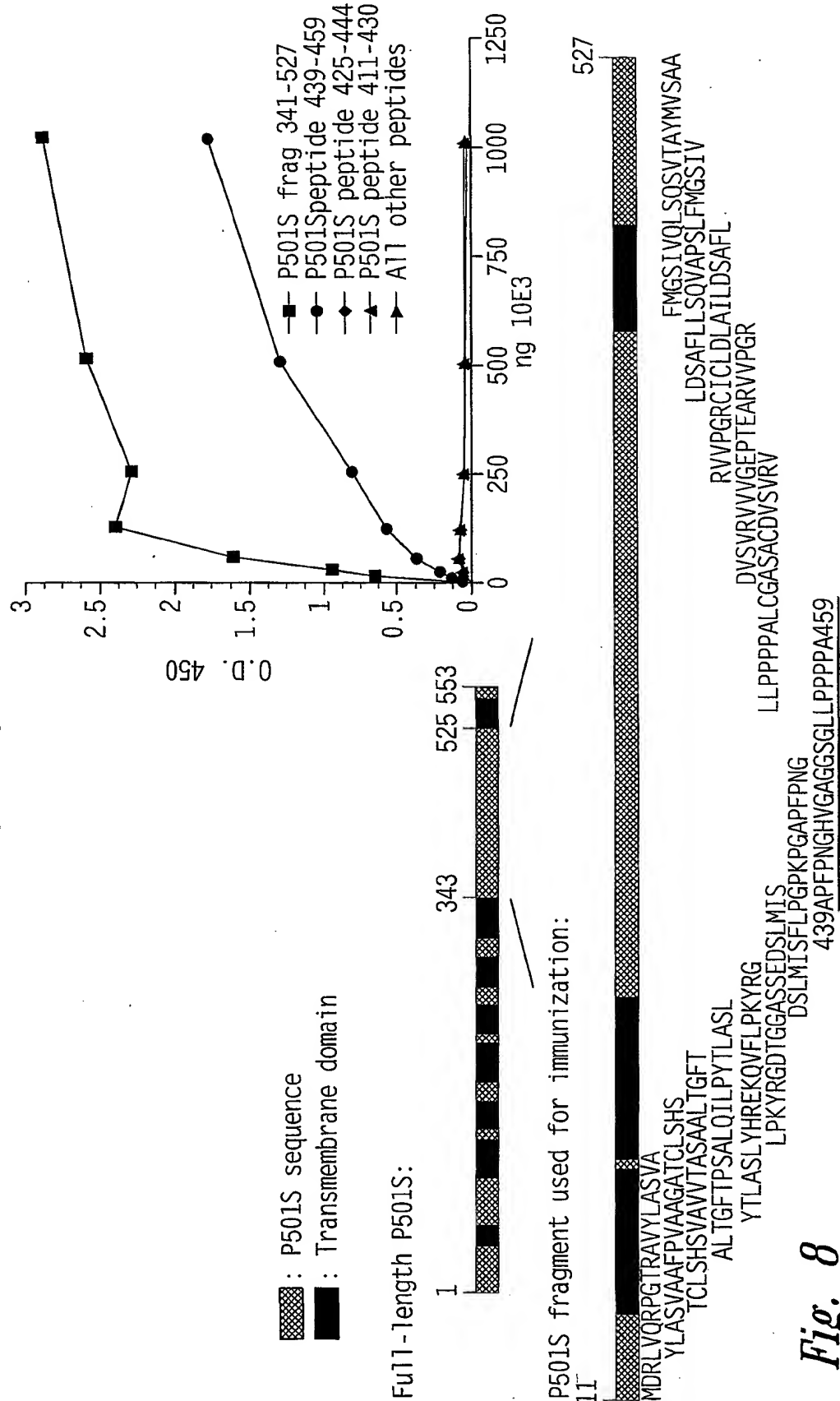


Fig. 8

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Schematic of P501S with predicted  
transmembrane, cytoplasmic, and extracellular regions

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TMVLGIGPVLGLVCYPLLGSAS

*DHWRGRYGRRRP* FIWALSLGILLSLFLIPRAGWL AGLLCPDPRPLE LALLILGVGLLDFCGQVCFTPL

*EALLSDLFRDPDHCRQ* AYSVYAFMISLGGCLGYLLPAI **DWDTSALAPYLGTEEE**

CLFGLLTLIFLTCVAATLLV AEEAALGPTEPAEGLSAPSLSPHCCPCRARLAFRNLGALLPRL

*HQLCCRMPTLR* LFVAELCSWMALMTFTLFYTD VGEGLYQGVPRAPGTEARRHYDEGVR

MGSLGLFLQCAISLVFSLVM DRLVQRFGTRAVYLAS VAAFPVAAGATCLSHSVAVVTA **SAA**

LTGFTFSALQILPYTLASLY *HREKQVFLPKYRGDTGGASSED* *SLMTSFLPGPKPGAPFPNGHVGAGGSGL*

*LPPPPALCGASACDVSVRVVVGEPTEARVVPGRG* ICLDLAILDSAFLLSQVAPSLF **MGSIVQLSQS**

VTAYMVSAAAGLGLVAIYFAT *QVVF* **DKSDLAKYSA**

Underlined sequence: Predicted transmembrane domain; **Bold sequence**:  
Predicted extracellular domain; *Italic sequence*: Predicted intracellular  
domain. Sequence in bold/underlined: used generate polyclonal rabbit  
serum

Localization of domains predicted using HMMTOP (G.E. Tusnady and I. Simon  
(1998) Principles Governing Amino Acid Composition of Integral Membrane  
Proteins: Applications to topology Prediction. J. Mol Biol. 283, 489-506.

*Fig. 9*

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Genomic Map of (5) Corixa Candidate Genes

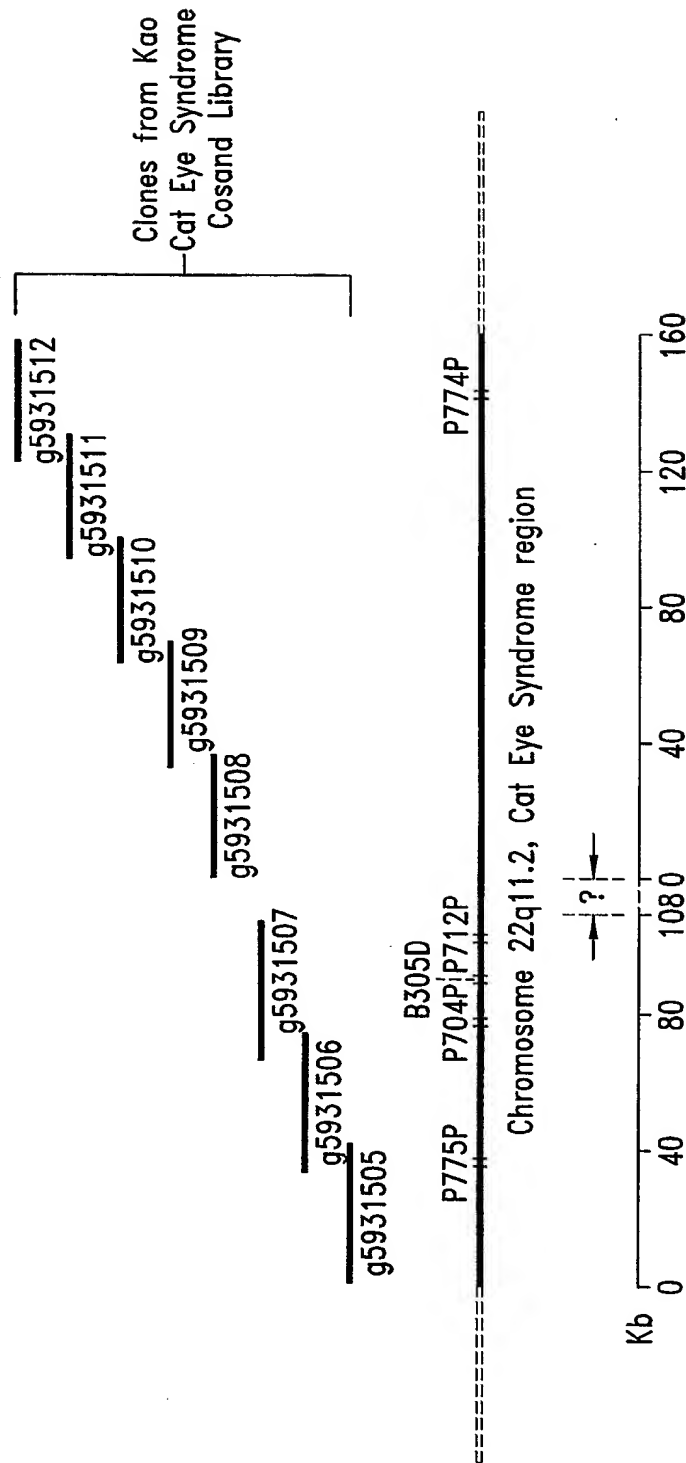
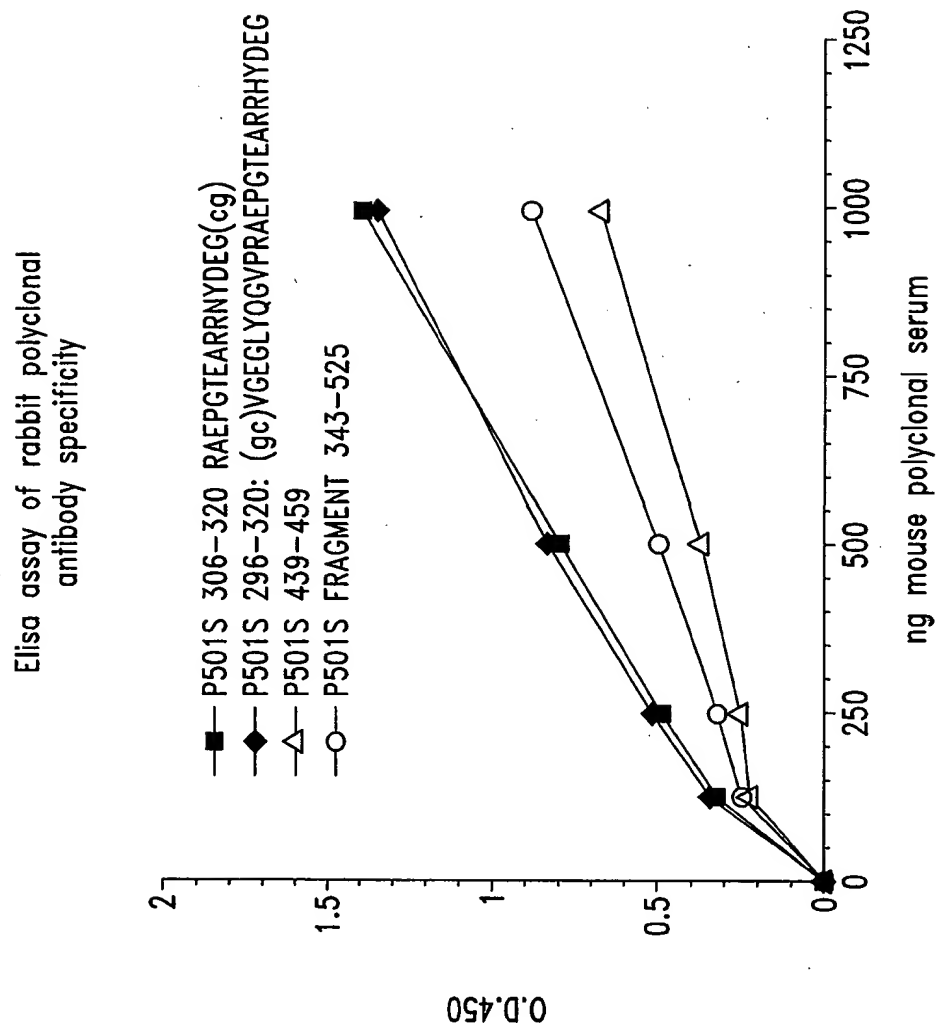


Fig. 10

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*Fig. 11*

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*Fig. 12A (1)*

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*Fig. 12A (2)*

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*Fig. 12A (3)*



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*Fig. 12B*

## SEQUENCE LISTING

<110> Corixa Corporation  
 Xu, Jiangchun  
 Dillon, Davin C.  
 Mitcham, Jennifer L.  
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 Kalos, Michael D.  
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 Day, Craig H.  
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 Carter, Darrick  
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 Henderson, Robert A.

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 gtgactggga aaaccctggg cgttaccaac ttaatcgctt tgcagcaat ccccttttcg 540  
 ccagctgggc gtaatancca aaaggcccg accgatcgcc ctccaacag ttgocacact 600  
 gaattgggnaa atgggacccc cctgtttacc cgcattnaac ccccgcnagg ttngttgtt 660  
 acccccacnt nnaccgctta cactttgcca gcgccttanc gccgcgtccc tttnccttt 720  
 cttcccttcc tttcnncncc ctttcccccg gggtttcccc cntcaaacc cna 773

<210> 4  
 <211> 828  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(828)  
 <223> n = A,T,C or G

<400> 4

cctcctgagt	cctactgacc	tgtgctttct	ggtgtggagt	ccagggctgc	taggaaaagg	60
aatgggcaga	cacaggtgta	tgccaatgtt	tctgaaatgg	gtataatttc	gtcctctcct	120
tcggaacact	ggctgtctct	gaagacttct	cgctcagttt	cagtgaggac	acacacaaaag	180
acgtgggtga	ccatgttggt	tgtgggggtgc	agagatggga	gggggtgggc	ccaccctgga	240
agagtggaca	gtgacacaag	gtggacactc	tctacagatc	actgaggata	agctggagcc	300
acaatgcatg	aggcacacac	acagcaagga	tgacnctgta	aacatagccc	acgtgtcct	360
gngggcactg	ggaagcctan	atnaggccgt	gagcanaaaag	aaggggagga	tccactagtt	420
ctanagcggc	cgccaccgcg	gtgganctcc	ancttttgtt	cccttttagtg	agggttaatt	480
gcgcgcttg	cntaatcatg	gtcatanctn	tttcctgtgt	gaaattgtta	tccgctcaca	540
attccacaca	acatacganc	cggaacata	aantgtaaac	ctgggggtgcc	taatgantga	600
ctaactcaca	ttaattgcgt	tgcgctcact	gcccgccttc	caatcnggaa	acctgtcttg	660
ccncttgcat	tnatgaatcn	gccaaacccc	ggggaaaagc	gtttgcgttt	tgggcgctct	720
tccgcttcct	cnctcantta	ntccctncnc	toggtcattc	cggctgcngc	aaaccgggtc	780
accnctcca	aaggggggtat	tccggtttcc	ccnaatccgy	gganancc		828

<210> 5  
 <211> 834  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(834)  
 <223> n = A,T,C or G

<400> 5

tttttttttt	tttttactga	tagatggaat	ttattaagct	tttcacatgt	gatagcacat	60
agtttttaatt	gcatccaaag	tactaacaaa	aactctagca	atcaagaatg	gcagcatgtt	120
atttttataac	aatcaacacc	tgtggctttt	aaaatttggt	tttcataaga	taattttatac	180
tgaagtaaat	ctagccatgc	ttttaaaaaa	tgcttttaggt	cactccaagc	ttggcagtta	240
acatttggtga	taaacaataa	taaaacaatc	acaatttaat	aaataacaaa	tacaacattg	300
tagggcataa	tcatatacag	tataaggaaa	aggtggtagt	gttgagtaag	cagttatttag	360
aatagaatac	cttggcctct	atgcaaatat	gtotagacac	tttgattcac	tcagccctga	420
cattcagttt	tcaaagtagg	agacaggttc	tacagtatca	ttttacagtt	tccaacacat	480
tgaaaaacaag	tagaaaaatga	tgagttgatt	tttattaatg	cattacatcc	tcaagagtta	540
tcaccaacccc	ctcagttata	aaaaattttc	aagttatatt	agtcataata	cttgggtgtgc	600
ttatttttaaa	ttagtgctaa	atggattaag	tgaagacaac	aatggtcccc	taatgtgatt	660
gatattggtc	atttttacca	gcttctaaat	ctnaactttc	aggcttttga	actggaacat	720
tgnatnacag	tgttccanag	ttncaaccta	ctggaacatt	acagtggtgct	tgattcaaaa	780
tggtatttttg	ttaaaaatta	aattttaacc	tggtggaaaa	ataatttgaa	atna	834

<210> 6  
 <211> 818  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(818)  
 <223> n = A,T,C or G

<400> 6

```

tttttttttt tttttttttt aagaccctca tcaatagatg gagacataca gaaatagtca      60
aaccacatct acaaaatgcc agtatcaggc ggcggcttcg aagccaaagt gatgtttgga      120
tgtaaagtga aatattagtt ggcggatgaa gcagatagtg aggaaagtgt agccaataat      180
gacgtgaagt ccgtggaagc ctgtggctac aaaaaatgtt gagccgtaga tgccgtcggg      240
aatggtgaag ggagactcga agtactctga ggcttgtagg agggtaaaat agagacccag      300
taaaattgta ataagcagtg cttgaattat ttggtttcgg ttgttttcta ttagactatg      360
gtgagctcag gtgattgata ctctgatgc gagtaatacg gatgtgttta ggagtgggac      420
ttctagggga tttagcgggg tgatgcctgt tgggggccag tgccctccta gttggggggt      480
aggggctagg ctggagtggg aaaaggctca gaaaaatcct gcgaagaaaa aaacttctga      540
ggtaataaat aggattatcc cgtatcgaag gcctttttgg acagggtggtg tgtggtggcc      600
ttggtatgtg ctttctcgtg ttacatcgcg ccatcattgg tatatggtta gtgtgttggg      660
ttantangg cttantatgaa gaacttttgg antggaatta aatcaatngc ttggccggaa      720
gtcattanga nggctnaaaa ggccctgtta ngggtctggg ctnggtttta ccnaccat      780
ggaatncccc ccccgaacna ntgnatccct attcttaa      818

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```

<210> 7
<211> 817
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(817)
<223> n = A,T,C or G

```

```

<400> 7
tttttttttt tttttttttt tggctctaga gggggtagag ggggtgctat agggtaaata      60
cgggccctat ttcaaagatt tttaggggaa ttaattctag gacgatgggt atgaaactgt      120
ggtttgctcc acagatttca gacgattgac cgtagtatac ccccgctcgt gtagcgtgga      180
aagtggtttg gtttagacgt ccgggaattg catctgtttt taagcctaata gtggggacag      240
ctcatgagtg caagacgtct tgtgatgtaa ttattatacn aatgggggct tcaatcggga      300
gtactactcg attgtcaacg tcaaggagtc gcaggtcgcc tggttctagg aataatgggg      360
gaagtatgta ggaattgaag attaatccgc cgtagtcggt gttctcctag gttcaatacc      420
attggtggcc aattgatttg atggttaagg gagggatcgt tgaactcgtc tgttatgtaa      480
aggatnccct ngggatggga aggcnatnaa ggactangga tnaatggcgg gcangattatt      540
tcaaacngtc tctanttoct gaaacgtctg aaatgttaat aanaattaan tttngttatt      600
gaatnttnng gaaaagggct tacaggacta gaaaccaaata angaaaanta atnntaangg      660
cnttatcntn aaaggtnata accnctccta tnatccacc caatngnatt cccacncnn      720
acnattggat nccccanttc canaaanggc cccccccgg tgnannccnc cttttgttcc      780
cttnantgan ggttattcnc cctngcntt atcancc      817

```

```

<210> 8
<211> 799
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(799)
<223> n = A,T,C or G

```

```

<400> 8
catttcggg tttactttct aaggaaagcc gagcggagc tgctaactgt ggaatcgggt      60
cataaggaga actttctgct ggcacgcgct agggacaagc gggagagcga ctccgagcgt      120
ctgaagcgca cgtcccagaa ggtggacttg gcaactgaaac agctgggaca catccgagag      180
tacgaacagc gcctgaaagt gctggagcgg gaggtccagc agtgtagccg cgtcctgggg      240
tgggtggccg angctganc cgctctgcct tgctgccccc angtgggccc ccacccctg      300
acctgcctgg gtccaaacac tgagccctgc tggcggactt caagganaac cccacangg      360

```

```

ggattttgct cctanantaa ggctcatctg ggccctcgcc ccccccactg gttggccttg 420
tctttgagnt gagcccatg tccatctggg ccactgtcng gaccaccttt ngggagtgtt 480
ctccttacaa ccacannatg cccggctcct cccggaaacc antccancc tnggaaggat 540
caagnccctgn atccactnnt nctanaaccg gccnccnccg cngtggaacc cnccttntgt 600
tccttttctnt tnagggttaa tnnccgcttg gccttncan ngtoctnnc nttttcnnt 660
gttnaaaattg ttangcnccc nccnntcccn cnnccnnan cccgaccn annntnnann 720
nccctgggggt nccnncngat tgaccenncc nccctntant tgenttnggg nncnntgccc 780
ctttccctct nggganncg 799

```

```

<210> 9
<211> 801
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(801)
<223> n = A,T,C or G

```

```

<400> 9
acgccttgat cctccaggc tgggactggt tctgggagga gccgggcatg ctgtgggttg 60
taangatgac actcccaaag gtggctcctga cagtggccca gatggacatg gggctcacct 120
caaggacaag gccaccaggt gcgggggccc aagcccatat gatccttact ctatgagcaa 180
aatcccctgt gggggcttct ccttgaagtc cgccancagg gctcagtctt tggaccang 240
caggtcatgg ggttgtnngc caactggggg ccncaacgca aaanggonca gggcctcngn 300
caccatccc angacgggc tacactnctg gacctccnc tccaccactt tcatgcgctg 360
ttentaccg cgnatntgtc ccantgttt cngtgcenac tccantttct nggacgtgcg 420
ctacatacgc ccggantcnc nctcccgctt tgtccctatc cactgnccan caacaaattt 480
cncctantg caccnattcc cacntttnc agntttcnc nncngcttc cttntaaaag 540
ggttganccc cggaaaatnc cccaaagggg gggggccngg tacccaactn cccctnata 600
gctgaantcc ccatnaccnn gntcnatgg anccntccnt ttaannacn ttctnaactt 660
gggaananc ctcgnccntn ccccnnttaa tccnccctg cnangnnct ccccnntcc 720
ncccnntng gentntnann cnaaaaaggc ccnnancaa tctcctnnn cctcanttgc 780
ccanccctcg aaatcggccn c

```

```

<210> 10
<211> 789
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(789)
<223> n = A,T,C or G

```

```

<400> 10
cagtctatnt ggccagtgtg gcagctttcc ctgtggctgc cggtgccaca tgcctgtccc 60
acagtgtggc cgtggtgaca gcttcagccg ccctcaccgg gttcaccttc tcagccctgc 120
agatcctgcc ctacacactg gcctccctct accaccggga gaagcagggt ttoctgccca 180
aataccgagg ggacactgga ggtgctagca gtgaggacag cctgatgacc agcttcctgc 240
caggccctaa gcctggagct cccttcccta atggacacgt ggggtgctgga ggcagtggcc 300
tgctcccacc tccaccgcg ctctgcgggg cctctgcctg tgatgtctcc gtacgtgtgg 360
tggtgggtga gccaccgan gccaggggtg ttccggggccg gggcatctgc ctggacctgc 420
ccatcctgga tagtgcttcc tgctgtccca ngtgggccca tccctgttta tgggctccat 480
tgtccagctc agccagtctg tcaactgccta tatggtgtct gccgcaggcc tgggtctggt 540
cccatttact ttgctacaca ggtantattt gacaagaacg anttggccaa atactcagc 600
ttaaaaaatt ccagcaacat tgggggtgga aggcctgcct cactgggtcc aactccccgc 660
tcctgttaac cccatggggc tgccggcttg gccgccaat tctgttgctg ccaaanntat 720

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gtggctctct gctgccacct gttgctggct gaagtgcnta cngcncanct ngggggggtng 780  
 ggngttccc 789

<210> 11  
 <211> 772  
 <212> DNA  
 <213> Homo sapien  
 <220>  
 <221> misc\_feature  
 <222> (1)...(772)  
 <223> n = A,T,C or G

<400> 11  
 cccaccctac ccaaataatta gacaccaaca cagaaaagct agcaatggat tcccttctac 60  
 ttgtgtaaata aaataagtta aatattttaa tgctgtgtc tctgtgatgg caacagaagg 120  
 accaacaggc cacatcctga taaaaggtaa gaggggggtg gatcagcaaa aagacagtgc 180  
 tgtgggctga ggggacctg ttcttgtgtg ttgcccctca ggactcttcc cctacaaata 240  
 actttcatat gttcaaatacc catggaggag tgtttcatcc tagaaactcc catgcaagag 300  
 ctacattaaa cgaagctgca ggttaagggg cttanagatg ggaaaccagg tgactgagtt 360  
 tattcagctc ccaaaaaccc ttctctaggt gtgtctcaac taggaggcta gctgttaacc 420  
 ctgagcctgg gtaatccacc tgcagagtcc ccgcattcca gtgcatggaa cccttctggc 480  
 ctccctgtat aagtccagac tgaaccccc ttggaaggnc tccagtcagg cagccctana 540  
 aactggggaa aaaagaaaa gacgccccan ccccagctg tgcanctacg cacctcaaca 600  
 gcacaggggtg gcagcaaaaa aaccacttta ctttggcaca aacaaaaact ngggggggca 660  
 accccggcac cccnangggg gttaacagga ancngggnaa cntggaaccc aattnaggca 720  
 ggccnccac ccnaatntt gctgggaaat ttttctccc cttaattntt tc 772

<210> 12  
 <211> 751  
 <212> DNA  
 <213> Homo sapien  
 <220>  
 <221> misc\_feature  
 <222> (1)...(751)  
 <223> n = A,T,C or G

<400> 12  
 gcccgaattc cagctgccac accacccacg gtgactgcat tagttcggat gtcatacaaa 60  
 agctgattga agcaaccctc tacttttttg tcgtgagcct tttgcttggg gcaggtttca 120  
 ttggctgtgt tgggtgacgtt gtcatcgcaa cagaatgggg gaaaggcact gttctctttg 180  
 aagtanggtg agtcctcaaa atccgtatag ttggtgaagc cacagcactt gagccctttc 240  
 atggtggtgt tccacacttg agtgaagtct tcctgggaac cataatcttt cttgatggca 300  
 ggcactacca gcaacgtcag ggaagtgtc agccattgtg gtgtacacca aggcgaccac 360  
 agcagctgcn acctcagcaa tgaagatgan gaggangatg aagaagaacg tcncgagggc 420  
 acacttgctc tcagtcttan caccatanca gcccntgaaa accaananca aagaccacna 480  
 cncggctgc gatgaagaaa tnacccnccg ttgacaaact tgcattggcac tggganccac 540  
 agtggcccn aaaaatcttca aaaaggatgc cccatcnatt gaccccccaa atgcccactg 600  
 ccaacagggg ctgccccacn cncnnaacga tganccnatt gnacaagatc tncntggtct 660  
 tnatnaacnt gaacctgcn tngtggctcc tggtcaggnc cnnngcctga cttctnaann 720  
 aangaactcn gaagncccca cngganannc g 751

<210> 13  
 <211> 729  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(729)  
 <223> n = A,T,C or G

<400> 13  
 gagccaggcg tccctctgcc tgcccactca gtggcaacac ccgggagctg ttttgcctt 60  
 tgtggancct cagcagtncc ctctttcaga actcantgcc aagancctg aacaggagcc 120  
 accatgcagt gcttcagctt cattaagacc atgatgatcc tcttcaattt gtcctcttt 180  
 ctgtgtggtg cagccctgtt ggcagtggtg atctgggtgt caatcgatgg ggcctcctt 240  
 ctgaagatct tcgggccact gtcgtccagt gccatgcagt ttgtcaacgt gggctacttc 300  
 ctcatgcag ccggcggtgt ggtcttagct ctaggtttcc tgggctgcta tgggtgctaag 360  
 actgagagca agtgtgccct cgtgacgttc ttcttcatcc tcctcctcat ctctattgct 420  
 gaggttgcaa tgctgtggtc gccttggtgt acaccacaat ggctgagcac ttctgacgt 480  
 tgctggtaat gcctgccatc aanaaaagat tatgggttcc caggaaact tcaactcaagt 540  
 gttggaacac caccatgaaa gggctcaagt gctgtggctt cnnccaacta tacggatttt 600  
 gaagantcac ctacttcaaa gaaaanagt cctttccccc atttctgttg caattgacaa 660  
 acgtcccaa cacagccaat tgaaaacctg caccacaacc aaanggtcc ccaaccanaa 720  
 attnaagg 729

<210> 14  
 <211> 816  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(816)  
 <223> n = A,T,C or G

<400> 14  
 tgctcttctt caaagttgtt cttgttgcca taacaaccac cataggtaaa gcgggcgag 60  
 tgctcgtga aggggttgta gtaccagcgc gggatgctct ccttgagag tcctgtgtct 120  
 ggcaggtcca cgcagtgccc tttgtcactg gggaaatgga tgcgctggag ctcgtaaaag 180  
 ccactcgtgt atttttcaca ggcagcctcg tccgacgcgt cggggcagtt gggggtgtct 240  
 tcacactcca ggaaactgtc natgcagcag ccattgctgc agcggaactg ggtgggctga 300  
 cangtgccag agcacactgg atggcgcctt tccatgnan gggccctgng ggaaagtccc 360  
 tganccccaan anctgcctct caaangcccc accttgacac ccccgacagg ctagaatgga 420  
 atcttcttcc cgaaaggtag ttnttcttgt tgcccaancc anccccntaa acaaactctt 480  
 gcanatctgc tccngggggg tcntantacc ancggtggaa aagaaccca ggngcgaac 540  
 caancttggt tggatncgaa gcnataatct nctnttctgc ttggtggaca gcaccantna 600  
 ctgtnnact ttagnccntg gtcctcntgg gttgnncttg aacctaatcn ccnntcaact 660  
 gggacaagggt aantngccnt ccttttaatt ccnancntn cccctggtt tggggttttn 720  
 cncnctccta cccagaaan nccgtgttcc ccccaacta ggggcnaaa ccnntnttc 780  
 cacaacctn cccacccac gggttcngnt gggtng 816

<210> 15  
 <211> 783  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(783)  
 <223> n = A,T,C or G

<400> 15  
 ccaaggcctg ggcaggcata nacttgaagg tacaaccca ggaaccctg gtgctgaagg 60



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atgtggaaaa cacagattgg cgcctactgc ggggtgacac ggatgtcagg gtagagagga 120
aagacccaaa ccaggtggaa ctgtggggac tcaaggaang cacctacctg ttccagctga 180
cagtgactag ctcagaccac ccagaggaca cggccaacgt cacagtcact gtgctgtcca 240
ccaagcagac agaagactac tgccctcgcat ccaacaangt gggtcgctgc cggggctctt 300
tcccacgctg gtactatgac cccacggagc agatctgcaa gagtttcgtt tatggaggct 360
gcttgggcaa caagaacaac taccttcggg aagaagagtg cattctancc tgtcnggggtg 420
tgcaaggtag gcctttgana ngcanctctg gggctcangc gactttcccc cagggccctt 480
ccatggaaag gcgccatcca ntgttctctg gcacctgtca gccacccag ttccgctgca 540
ncaatggctg ctgcacnac antttcctng aattgtgaca acacccccca ntgcccccaa 600
ccctcccaac aaagcttccc tgttnaaaaa tacnccantt ggcttttnac aaacncccg 660
cncctcctt ttcccnntn aacaaagggc nctngcctt gaactgccn aaccnngaa 720
tctnccnng aaaaantncc cccctgggt cctnnaanc cctcncnaa anctncccc 780
ccc 783

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<210> 16
<211> 801
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(801)
<223> n = A,T,C or G

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```

<400> 16
gccccaatc cagctgccac accaccacag gtgactgcat tagttcggat gtcatacaaa 60
agctgattga agcaaccctc tacttttttg tcgtgagcct tttgcttggg gcaggtttca 120
ttggctgtgt tgggtacgtt gtcattgcaa cagaatggg gaaaggcact gttctctttg 180
aagtaggggt agtcctcaaa atccgtatag ttggtgaagc cacagcactt gagccctttc 240
atgggtgtgt tccacacttg agtgaagtct tccctgggaac cataatcttt cttgatggca 300
ggcactacca gcaacgtcag gaagtgtcga gccattgtgg tgtacaccaa ggcgaccaca 360
gcagctgcaa cctcagcaat gaagatgagg aggaggatga agaagaacgt cncgagggca 420
cacttgctct ccgtcttagc accatagcag cccangaaac caagagcaaa gaccacaacg 480
cngctgcga atgaaagaaa ntaccacagt tgacaaactg catggccact ggacgacagt 540
tgcccgaan atcttcagaa aagggtgcc ccatcgattg aacaccana tgcccactgc 600
cnacagggct gcncncnncn gaaagaatga gccattgaag aaggatcctc ntgggtcttaa 660
tgaactgaaa cntgcatgg tggccctgt tccagggtct tggcagtga ttctganaaa 720
aaggaacngc nttagcccc ccaaangana aaacaccccc ggggtgtgcc ctgaattggc 780
ggccaaggan cctgccccn g 801

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```

<210> 17
<211> 740
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(740)
<223> n = A,T,C or G

```

```

<400> 17
gtgagagcca ggcgtccctc tgccctgcca ctcagtggca acaccggga gctgttttgt 60
cctttgtgga gcctcagcag ttccctcttt cagaactcac tgccaagagc cctgaacagg 120
agccaccatg cagtgttca gcttcattaa gaccatgatg atcctcttca atttgctcat 180
ctttctgtgt ggtgcagccc tgttggcagt gggcatctgg gtgtcaatcg atggggcatc 240
ctttctgaag atcttcgggc cactgtcgtc cagtgcacat cagtttgtca acgtgggcta 300
cttcctcatc gcagccggcg ttgtggtctt gctccttggg ttccctgggt gctatggtgc 360
taagacggag agcaagtgtg ccctcgtgac gttcttcttc atcctcctcc tcctctcat 420

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tgctgaagtt	gcagctgctg	tggtgcgctt	ggtgtacacc	acaatggctg	aaccattcct	480
gacgttgctg	gtantgcctg	ccatcaanaa	agattatggg	ttcccaggaa	aaattcactc	540
aantntggaa	caccnccatg	aaaagggctc	caatttctgn	tggttcccc	aactataccg	600
gaattttgaa	agantcnccc	tacttccaaa	aaaaaanant	tgcttttnc	ccnttctgt	660
tgcaatgaaa	acntcccaan	acngccaatn	aaaacctgcc	cnnncaaaaa	ggntcncaaa	720
caaaaaaant	nnaagggttn					740

<210> 18  
 <211> 802  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(802)  
 <223> n = A,T,C or G

<400> 18	
ccgctgggtt	cgctgggtcca gngnagccac gaagcacgtc agcatacaca gcctcaatca 60
caaggtcttc	cagctgcccgc acattacgca gggcaagagc ctccagcaac actgcatatg 120
ggatacactt	tacttttagca gccagggtga caactgagag gtgtcgaagc ttattcttct 180
gagcctctgt	tagtggagga agattccggg cttcagctaa gtagtcagcg tatgtcccat 240
aagcaaacac	tgtgagcagc cggaaggtag aggcaaagtc actctcagcc agctctctaa 300
cattgggcat	gtccagcagt tctccaaaca cgtagacacc agnggcctcc agcacctgat 360
ggatgagtgt	ggccagcgct gcccccttgg ccgacttggc taggagcaga aattgctcct 420
ggttctgccc	tgtcaccttc acttcgcac tcactactgc actgagtgtg ggggacttgg 480
gctcaggatg	tccagagacg tggttccgcc ccctcnctta atgacaccgn ccanncaacc 540
gtcggctccc	gccgantgng ttcgtcgtnc ctgggtcagg gtctgctggc cnctacttgc 600
aanccttgc	nggcccatgg aattcaccnc accggaactn gtangatcca ctntttctat 660
aaccggncgc	caccgcnnnt ggaactccac tcttnttnc tttacttgag ggttaaggtc 720
acccttnncg	ttaccttggg ccaaaccntn cnttgtgtcg anantngtna tcnngnccna 780
tnccanccnc	atangaagcc ng

<210> 19  
 <211> 731  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(731)  
 <223> n = A,T,C or G

<400> 19	
cnaagcttcc	aggtnacggg ccgcnanacc tgaccnagg tancanaang cagnncggcg 60
gagcccaccg	tcacgnggng gngtctttat nggagggggc ggagccacat cnctggacnt 120
cntgacccca	actcccncnc nncantgca gtgatgagtg cagaactgaa ggtnacgtgg 180
caggaaccac	gancaaannc tgctccnntc caagtccgcn nagggggcg ggtggccac 240
gncatccnt	cnagtgtctg aaagcccnnc cctgtctact tgtttggaga acngcnnga 300
catgccagc	gttanataac nggcnagag tnantttgcc tctcccttcc ggtgcgcan 360
cgngtntgct	tagnggacat aacctgacta cttaactgaa ccnngaata tncnccct 420
ccactaagct	cagaacaaaa aacttcgaca ccactcantt gtcacctgnc tgctcaagta 480
aagtgtaccc	catncccaat gtntgctnga ngtctgncc tgcnttangt tcggtcctgg 540
gaagacctat	caattnaagc tatgtttctg actgcctctt gctccctgna acaancnacc 600
cnncnntcca	agggggggnc ggccccaat cccccaacc ntnaattnan ttancccn 660
ccccnggcc	cggcctttta cnanctcnn nnacngggna aaaccnnngc tttncccaac 720
nnaatccncc	t

<210> 20  
 <211> 754  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(754)  
 <223> n = A,T,C or G

<400> 20  
 tttttttttt tttttttttt taaaaacccc ctccattnaa tgnaaacttc cgaaattgtc 60  
 caacccctc ntccaaatnn ccttttcgg gngggggttc caaacccaan ttanntttgg 120  
 annttaaatt aaatnttnt tggnggnna anccnaatgt nangaaagtt naaccanta 180  
 tnancttnaa tncctggaaa cngtngntt ccaaaaatnt ttaaccctta antccctccg 240  
 aaatngttna nggaaaaccc aantttctnt aaggttggtt gaaggntnaa tnaaaanccc 300  
 nnccaattgt ttttngccac gcctgaatta attggnttcc gntgttttcc nttaaaanaa 360  
 gggnancccc ggttantnaa tcccccnnc cccaattata ccganttttt ttngaattgg 420  
 gancccnccg gaattaacgg ggnnnntccc tnttgggggg cnggnncccc cccntcggg 480  
 ggttnggnc agnncnaat tgttaaggg tccgaaaaat cctccnaga aaaaanctc 540  
 ccaggntgag nntnggggtt ncccccccc canggccct ctcgnanagt tggggttgg 600  
 ggggcctggg attttntttc cctnttnc tcccccccc cnggganag aggttngngt 660  
 tttgntcnc ggcccnccn aagantttt ccganttnan ttaaaccnt gcctnggcga 720  
 agtcnttgn agggntaan ggccccctnn cggg 754

<210> 21  
 <211> 755  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(755)  
 <223> n = A,T,C or G

<400> 21  
 atcancccat gacccnaac nngggaccnc tcancgggnc nnncnaccnc cggccnatca 60  
 nngtnagnnc actncnntn natcacnccc cncnactac gccncnanc cnacgcnta 120  
 nncanatncc actganngcg cngtngan ngagaaact nataccanag ncaccanacn 180  
 ccagctgtcc nanaangcct nnnatacngg nnnatccaat ntgnancctc cnaagtattn 240  
 nncnncanact gattttcctn anccgattac cctncccc tanccctcc ccccaacna 300  
 cgaaggcnct ggnccnaagg nngcgnccc ccgctagntc cccncaagt cncnccta 360  
 aactcancn nattaacngc ttcntgagta tcaactcccg aatctcacc tactcaactc 420  
 aaaaanactn gatacaaat aatncaagcc tgnttatnac actntgactg ggtctctatt 480  
 ttagnngtcc ntanaancnt ctaatacttc cagtctnct tcnccaattt cnaangget 540  
 ctttcngaca gcatntttt gttcccnntt gggttcttan ngaattgcc ttcntngaac 600  
 gggctcctt tttccttcgg ttancctggg ttcnccggc cagttattat ttccntttt 660  
 aaattcctnc cntttanttt tggccttca aacccccggc cttgaaaacg gcccctggt 720  
 aaaaggttgt tttganaaaa tttttgttt gtcc 755

<210> 22  
 <211> 849  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(849)

<223> n = A,T,C or G

<400> 22

tttttttttt	tttttangtg	tngtcgtgca	ggtagaggct	tactacaant	gtgaanacgt	60
acgctnggan	taangcgacc	cganttctag	gannncacct	aaaatcanac	tgtgaagatn	120
atcctgnnna	cggaanggtc	accggnngat	nntgctaggg	tgneenctcc	cannncnttn	180
cataactcng	nggccctgcc	caccaccttc	ggcgggccng	ngnccggggc	cgggtcattn	240
gnnttaaccn	cactnngcna	ncggtttccn	ccccenncng	accnnggcga	tccgggggtnc	300
tctgtcttcc	cctgnagncn	anaaantggg	ccnccggnccc	ctttaccctt	nnacaagcca	360
cngcctctta	ncnccngccc	cccctccant	nngggggact	gccnanngct	ccgttntctng	420
nnaccccnnn	gggtncctcg	gttgctcgant	cnaccgnang	ccanggattc	cnaaggaagg	480
tgcgttnttg	gcccctaccc	ttcgtctnccg	nnccaccttc	ccgacnanga	nccgctcccg	540
cncnccgnng	cctcncctcg	caacaccgcg	ntctctcngt	ncggnnnccc	cccacccgc	600
ncctctcnc	ngnccgnancn	ctccnccncc	gtctcannca	ccaccccgcc	ccgccaggcc	660
ntcanccacn	ggngacnng	nagcncnttc	gncccgcgc	gcgncnccct	cgcncngaa	720
ctnctctngg	ccantnncgc	tcaancnna	cnaaacgcg	ctgcgcggcc	cgnagcgncc	780
ncctccncca	gtcctcccg	cttccnacc	angnnttccn	cgaggacacn	nnaccccgcc	840
nncangcgg						849

<210> 23

<211> 872

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(872)

<223> n = A,T,C or G

<400> 23

gcgcaaaacta	tacttcgctc	gnactcgtgc	gcctcgtcnc	tcttttcctc	cgcaaccatg	60
tctgacnanc	ccgattnggc	ngatatchan	aagntcganc	agtccaaact	gantaacaca	120
cacacnncan	aganaaatcc	netgccttcc	anagtanacn	attgaacnng	agaaccangc	180
nggcgaatcg	taatnaggcg	tgcgccgcc	atntgtcncc	gtttattntn	ccagctcnc	240
ctnccnacc	tactctctcn	nagctgtcnn	accctngtn	cgnaccccc	naggtcgga	300
tcgggttttn	nntgaccgng	cnccccctcc	ccccctccat	nacganccnc	ccgcaccacc	360
nanngcncgc	cccccgnnct	cttcgcnc	ctgtcctntn	ccccgtngc	ctggcncngn	420
accgcattga	ccctcgcnn	ctncnngaaa	ncgnanacgt	ccgggttggn	annancgctg	480
tgggnnngcg	tctgcncgc	gttccttccn	ncncttcca	ccatcttct	tacnggtct	540
ccnccgctc	tcnncaacnc	cctgggacgc	tnctctntgc	cccccttnac	ccccccctt	600
cgncgtgncc	cgnccccacc	ntcatttnca	nacgntcttc	acaannncct	ggntnctcc	660
cnancngnnc	gtcancnag	ggaaggngg	ggnnccnntg	nttgacgttg	ngngangtc	720
cgaanantcc	tcnccntcan	cnctaccct	cgggcgnnct	ctcngttnc	aacttancaa	780
ntctcccccg	ngngcncntc	tcagcctcnc	ccccccnct	ctctgcantg	tnctctgctc	840
tnaccnntac	gantnttcgn	cncctcttt	cc			872

<210> 24

<211> 815

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(815)

<223> n = A,T,C or G

<400> 24

gcattgcaagc	ttgagtattc	tatagngtca	cctaaatanc	ttggcntaat	catggtcnta	60
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```
<210> 25
<211> 775
<212> DNA
<213> Homo sapien
```

```
<220>
<221> misc_feature
<222> (1)...(775)
<223> n = A,T,C or G
```

<400> 25							
ccgagatgtc	tcgctccgtg	gccttagctg	tgctcgcgct	actctctctt	tctggcctgg	60	
aggctatcca	gcgtactcca	aagattcagg	tttactcacg	tcattccagca	gagaatggaa	120	
agtcaaattt	cctgaattgc	tatgtgtctg	ggtttcatcc	atccgacatt	gaanttgcct	180	
tactgaagaa	tgganagaga	attgaaaaag	tgagcattc	agacttgtct	ttcagcaagg	240	
actggtcttt	ctatctcntg	tactacactg	aattcacccc	cactgaaaaa	gatgagtatg	300	
cctgcgctgt	gaaccatgtg	actttgtcac	agcccaagat	agttaagttg	gatcgagaca	360	
tgtaagcagn	cnncatggaa	gtttgaagat	gccgcatttg	gattggatga	attccaaatt	420	
ctgcttgctt	gcnttttaat	antgatatgc	ntatacaccc	taccctttat	gnccccaat	480	
tgtaggggtt	acatnantgt	tcncntngga	catgatcttc	ctttataant	ccnccnttcg	540	
aattgcccg	cncncngttt	ngaattgttc	cnnaaccacg	gttggtctcc	ccaggtcncc	600	
tcttacggaa	gggcctgggc	cnccttncaa	ggttggggga	accnaaaatt	tcnctnttgc	660	
ccnccncca	cnnctcttng	nnncnctatt	ggaacccttc	cnattccctt	tggcctcnna	720	
nccttnncta	anaaaactng	aaancgtngc	naaanntttt	acttcccccc	ttacc	775	

```
<210> 26
<211> 820
<212> DNA
<213> Homo sapien
```

```
<220>  
<221> misc_feature  
<222> (1)...(820)  
<223> n = A,T,C or G
```

<400> 26						
anattantac	agtgtaatct	tttcccagag	gtgtgtanag	ggaacggggc	ctagaggcat	60
cccanagata	ncttatanca	acagtgtctt	gaccaagagc	tgctgggcac	atttcttgca	120
gaaaaggtgg	cgggtcccat	cactcctcct	ctcccatagc	catcccagag	gggtgagtag	180
ccatcangcc	ttcggtgggg	gggagtcang	gaaacaacan	accacagagc	anacagacca	240
ntgatgacca	tgggcggggg	cgagcctctt	ccctgnaccg	gggtggcana	nganagccta	300
nctgaggggt	cacactataa	acgttaaacg	ccnagatnan	cacctgcttc	aagtgacccc	360
ttctactctg	acnaccagng	accnnnaact	gcngcctggg	gacagcncctg	ggancagcta	420
acnnagcact	cacctgcgcc	cccatgqccq	tnccgntccc	tggtcctgnc	aaqggaagct	480

```

ccctgttgga attncgggga naccaaggga nccccctcct ccactgtga aggaaaaann 540
gatggaattt tnccttccg gccnntcccc tcttccttta cagccccct nntactctc 600
tccctctntt ntccgtncnc acttttnacc cennnatitc ccttnattga tcggannctn 660
ganattccac tnnccgctnc cntcnatcng naanacnaaa nactntctna cccnggggat 720
gggnnccctg ntcactcctc ctttttctct accnccnntt ctttgccctc ccttngatca 780
tccaacctc gntggccntn ccccccnntt tcttttnc 820

```

```

<210> 27
<211> 818
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(818)
<223> n = A,T,C or G

```

```

<400> 27
tctgggtgat ggcctcttcc tcctcaggga cctctgactg ctctgggcca aagaatctct 60
tgtttcttct ccgagcccca gccagcgggtg attcagccct gcccaacctg attctgatga 120
ctgcggtatg tgtgacggac ccaaggggca aatagggtcc caggggtccag ggaggggagc 180
ctgctgagca cttccgcccc tcaacctgcc cagccccctg catgagctct gggctgggtc 240
tccgcctcca gggttctgct cttccangca ngccancaag tggcgtggg ccacactggc 300
ttcttctctg cccntccctg gctctganc tctgtcttcc tgtcctgtgc angcnccttg 360
gatctcagtt tccctcctc anngaactct gttcttgann tcttcantta actntgantt 420
tatnacnna tggnctgtnc tgcnnactt taatgggccc gaccggctaa tccctccctc 480
nctcccttcc anttccnna accngcttnc cntctctcc cntancccg ccngggaanc 540
ctcctttgcc ctnaccang gccnnnaccg cccntnnctn ggggggcnng gtnnctncnc 600
ctgntnnccc cncctcncnt tncctcgtcc cncnncgc nngcannttc ncngtcccn 660
tnnctcttcc ngntcgnaa ngntcncntn tnnnnngnc ngntnntn tccctctcnc 720
cnnntgnang tnnntnnnc ncngncccc nnnnnnnnn nggnntnnn tctnncngc 780
ccnncccc ngnattaagg cctccnntct ccggccnc 818

```

```

<210> 28
<211> 731
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(731)
<223> n = A,T,C or G

```

```

<400> 28
aggaaggcgg gagggatatt gtangggatt gagggatagg agnataangg gggaggtgtg 60
tcccaacatg anggtgnngt tctcttttga angagggttg ngtttttann ccnggtgggt 120
gattnaaccc cattgtatgg agnnaaagg ttttagggat ttttcggctc ttatcagtat 180
ntanattcct gtnaatcgga aaatnatntt tcnnncggaa aatnttgctc ccatccgnaa 240
atttctccg ggtagtgc tntnggggn cngccangtt tcccaggctg ctanaatcgt 300
actaaagntt naagtggan tncaaatgaa aacctnnac agagnatccn taccgactg 360
tnnnttncct tgcctctntg actctgcng agcccaatac ccnngngnat gtcncccn 420
nnngcgcnc tgaaannnc tcnnggctnn gancatcang gggtttcgca tcaaaagcnn 480
cgtttcncat naaggcact tngcctcat caaccnctng cctcnmcca tttngccgtc 540
nggttncct acgctnntng cncctnnntn ganattttnc ccgcctngg naancctcct 600
gnaatgggta gggnccttntc ttttnaccnn gnggtntact aatcnctnc acgcntnctt 660
tctnaccccc ccccttttt caatccanc ggcnaatgg gtctcccn cgangggggg 720
nnnccann c 731

```

14

<210> 29  
 <211> 822  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(822)  
 <223> n = A,T,C or G

<400> 29  
 actagtccag tgtggtggaa ttccattgtg ttggggncnc ttctatgant antnttagat 60  
 cgctcanacc tcacancctc ccnacnangc ctataangaa nannaataga nctgtncnnt 120  
 atntntacnc tcatanncct cmnacccac tccctcttaa cccntactgt gcctatngcn 180  
 tnnctantct ntgcgcctn cnanccaccn gtgggccnac cncnngnatt ctcnatctcc 240  
 tcnccatntn gcctananta ngtncatacc ctatacctac nccaatgcta nnnctaancn 300  
 tccatnantt annntaacta ccaactgacnt ngactttcnc atnanctcct aatttgaatc 360  
 tactctgact cccacngcct annnattagc ancntccccc nacnatntct caaccaaadc 420  
 ntcaacaacc tatctantctg ttcnccaacc nttncctccg atccccnnac aacccccctc 480  
 ccaaataccc nccacctgac nccaaaccn caccatcccg gcaagccnan ggcatttan 540  
 ccaactggaat cacnatngga naaaaaaac ccnaactctc tancncnnat ctccctaana 600  
 aatnctcctn naatttactn ncantnccat caanccacn tgaaacnnaa cccctgtttt 660  
 tanatccctt ctttcgaaaa ccnacccttt annncccaac ctttngggcc ccccnctnc 720  
 ccnaatgaag gncncccaat cnangaaacg nccntgaaaa ancnaaggcna anannntccg 780  
 canatcctat cccttanttn ggggnccctt ncccnngggc cc 822

<210> 30  
 <211> 787  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(787)  
 <223> n = A,T,C or G

<400> 30  
 cgggcgcctg ctctggcaca tgcctcctga atggcatcaa aagtgatgga ctgcccattg 60  
 ctagagaaga ccttctctcc tactgtcatt atggagccct gcagactgag ggctcccctt 120  
 gtctgcagga tttgatgtct gaagtcgttg agtgtggctt ggagctcctc atctacatna 180  
 gctggaagcc ctggagggcc tctctcgcca gcctccccct tctctccag ctctccangg 240  
 acaccagggg ctocaggcag cccattattc ccagnangac atgggtgttc tccacgcgga 300  
 cccatggggc ctgnaaggcc agggctcctt ttgacaccat ctctcccgtc ctgcctggca 360  
 ggccgtggga tccactantt ctanaacggn cgccaccncg gtgggagctc cagcttttgt 420  
 tcccnttaat gaaggttaat tgcncgcttg gcgtaatcat nggtcanaac tntttcctgt 480  
 gtgaaattgt ttntccctc ncnatccnc ncnacatacn aaccgggaan cataaagtgt 540  
 taaagcctgg gggtnccctn nngaataaac tnaactcaat taattgcgtt ggctcatggc 600  
 ccgctttccn ttcnggaaaa ctgtctctcc ctgcnttntt gaatcgcca ccccnnggg 660  
 aaaagcggtt tgcnttttng ggggntcctt ccncttccc cctcnctaan cctnccgct 720  
 cggtcgttnc nggtngcggg gaangggnat nnnctccnc naaggggng agnnngntat 780  
 ccccaaa 787

<210> 31  
 <211> 799  
 <212> DNA  
 <213> Homo sapien

<220>

15

<221> misc\_feature  
 <222> (1)...(799)  
 <223> n = A,T,C or G

<400> 31  
 tttttttttt ttttttttgc gatgctactg ttttaattgca ggaggtgggg gtgtgtgtac 60  
 catgtaccag ggctattaga agcaagaagg aaggaggagg ggcagagcgc cctgctgagc 120  
 aacaaaggac tcctgcagcc ttctctgtct gtctcttggc gcaggcacat ggggaggcct 180  
 cccgcagggt gggggccacc agtccagggt tgggagcact acanggggtg ggagtgggtg 240  
 gtggctggtg cnaatggcct gncacanatc cctacgattc ttgacacctg gatttcacca 300  
 ggggaccttc tgttctccca nggnaacttc nttnatctcn aaagaacaca actgtttctt 360  
 cngcanttct ggctgttcat ggaaagcaca ggtgtccnat ttnggctggg acttggtaca 420  
 tatggttccg gcccacctct cccntcnaaa aagtaattca ccccccccn cctctnttg 480  
 cctgggccct taantaccca caccggaact canttantta ttcatcttng gntgggcttg 540  
 nttnatcncn cctgaangcg ccaagttgaa aggccacgcc gtncncnctc cccatagnan 600  
 nttttnnnt canctaatagc cccccnggc aacnatcaa tcccccccn tgggggcccc 660  
 agccanggc ccccgncctg ggnnccngn cncgnantcc ccaggntctc ccantcngnc 720  
 ccnnngcnc cccgcacgca gaacanaagg ntngagccnc cgcannnnnn nggtnnncac 780  
 ctcgcccccc ccnncgng 799

<210> 32  
 <211> 789  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(789)  
 <223> n = A,T,C or G

<400> 32  
 tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 60  
 ttttncnag ggcaggttta ttgacaacct cncgggacac aancaggctg gggacaggac 120  
 ggcaacaggc tccggcgggc gggcgggcgg ccctacctgc ggtaccaaata ntgcagcctc 180  
 cgctcccgt tgatnttccct ctgcagctgc aggatgcctt aaaaacagggc ctcgcccntn 240  
 ggtgggcacc ctgggatttn aatttccacg ggcacaatgc ggtcgcancc cctcaccacc 300  
 nattaggaat agtggtnnta cccncnccg ttggcncact cccntggaa accacttntc 360  
 ggggtcccg catctggtct taaaccttgc aaacnctggg gccctctttt tggttantnt 420  
 nccngccaca atcatnactc agactggcnc gggtggccc caaaaaancn ccccaaaacc 480  
 ggnccatgtc ttncgggggt tgctgcnatn tncatcacct cccgggcnc naaggncac 540  
 ccaaaagttc ttgnggccc caaaaaanct ccggggggnc ccagtttcaa caaagtcac 600  
 ccccttggcc cccaaatcct cccccgntt nctgggtttg ggaacccacg cctctnnctt 660  
 tggngggcaa gntggntccc ccttcgggcc cccggtgggc ccnctctaa ngaaaacncc 720  
 ntctnnnca ccatcccccc nngnnacgnc tancaangna tccctttttt tanaaacggg 780  
 cccccncc 789

<210> 33  
 <211> 793  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(793)  
 <223> n = A,T,C or G

<400> 33  
 gacagaacat gttggatggt ggagcacctt tctatacgac ttacaggaca gcagatgggg 60



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aattcatggc tgttggagca atanaacccc agttctacga gctgctgac aaaggacttg 120
gactaaagtc tgatgaactt cccaatcaga tgagcatgga tgattggcca gaaatgaana 180
agaagtttgc agatgtattt gcaaagaaga cgaaggcaga gtggtgtcaa atctttgacg 240
gcacagatgc ctgtgtgact ccggttctga cttttgagga ggttggtcat catgatcaca 300
acaangaacg gggctcgttt atcaccantg aggagcagga cgtgagcccc cgccctgcac 360
ctctgctggt aaacacccca gccatccctt ctttcaaaag ggatccacta cttctagagc 420
ggncgccacc gcggtggagc tccagctttt gttcccttta gtgagggtta attgcgcgct 480
tggcgtaate atggtcatan ctgtttctg tgtgaaattg ttatccgctc acaattccac 540
acaacatacg anccggaagc atnaaattt aaagcctggn ggtngcctaa tgantgaact 600
nactcacatt aattggcttt gcgctcactg cccgctttcc agtccggaaa acctgtcctt 660
gccagctgcc nttaatgaat cnggccaccc cccggggaaa aggcngtttg cttnttgggg 720
cgcncttccc gctttctcgc ttctgaant ccttcccccc ggtctttcgg cttgcccna 780
acggtatcna cct 793

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<210> 34
<211> 756
<212> DNA
<213> Homo sapien

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<220>
<221> misc_feature
<222> (1)...(756)
<223> n = A,T,C or G

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<400> 34
gccgcgaccg gcatgtacga gcaactcaag ggcgagtga accgtaaaag cccaatctt 60
ancaagtgcg gggaanagct gggtcgactc aagctagtct ttctggagct caacttcttg 120
ccaaccacag ggaccaagct gaccaaacag cagctaattc tggcccgta catactggag 180
atcggggccc aatggagcat cctacgcaan gacatccct ccttcgagcg ctacatggcc 240
cagctcaaat gctactactt tgattacaan gagcagctcc ccgagtcagc ctatatgcac 300
cagctcttgg gcctcaacct cctcttctg ctgtcccaga accgggtggc tgantnccac 360
acgganttgg ancggtgcc tgcccanga catacanacc aatgtctaca tcnaccacca 420
gtgtcctgga gcaatactga tgganggcag ctaccncaaa gtnttcttg ccnagggtaa 480
catcccccg cgagagctac accttcttca ttgacatcct gctcgacact atcagggatg 540
aaaatcgcn ggttgcctca gaaaggctnc aanaanatcc ttttcnctga aggcccccgg 600
atncnctagt nctagaatcg gcccgccatc gcggtgganc ctccaacctt tcgttnccct 660
ttactgaggg ttnattgccg cccttgccgt tatcatggtc acnccngttn cctgtgttga 720
aattnttaac cccccacaat tccacgcna cattng 756

```

```

<210> 35
<211> 834
<212> DNA
<213> Homo sapien

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```

<220>
<221> misc_feature
<222> (1)...(834)
<223> n = A,T,C or G

```

```

<400> 35
gggatctct anactnacct gnatgcatgg ttgtcgggtg ggtcgtgtc gatgaanatg 60
aacaggatct tgcccttgaa gctctcggt gctgtnttta agttgctcag tctgccgtca 120
tagtcagaca cnetcttggg caaaaaacan caggatntga gtcttgattt cacctccaat 180
aatcttcngg gctgtctgct cggtagaact gatgacnang ggcagctggg tgtgtntgat 240
aaantccanc angttctcct tggtagctc cccttcaaaag ttgttccggc cttcatcaaa 300
cttctnnaan angannancc canctttgtc gagctggnat ttgganaaca cgtcactgtt 360
ggaactgat cccaaatgg atgtcatcca tcgctctgc tgcctgcaaa aaacttgctt 420
ggcncaaatc cgactcccn tccttgaaag aagccnatca caccctcct cctggactcc 480

```

nncaangact	ctnccgctnc	cccntccnng	caggggttggt	ggcannccgg	gcccntgcgc	540
ttcttcagcc	agttcacnat	nttcatcagc	ccctctgcc	gctgttntat	tccttggggg	600
ggaanccgctc	tctcccttcc	tgaannaact	ttgaccgtng	gaatagccgc	gcntcncnt	660
acntnctggg	ccgggttcaa	antccctccn	ttgncnntcn	cctcggggcca	ttctggattt	720
nccnaacttt	ttccttcccc	cnccccnccg	ngtttggnnt	tttcatnggg	ccccaactct	780
gctnttgccc	antcccttgg	gggcntntan	cnccccctnt	ggtcccntng	ggcc	834

<210> 36  
 <211> 814  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(814)  
 <223> n = A,T,C or G

<400> 36						
cggnccgcttt	cngccgcgc	cccgtttcca	tgacnaaggc	tccttccang	ttaaatacnn	60
cctagnaaac	attaatgggt	tgctctacta	atacatcata	cnaaccagta	agcctgccca	120
naacgccaac	tcaggccatt	cctaccaaag	gaagaaaggc	tggtctctcc	acccctgta	180
ggaaaggcct	gccttgtaag	acaccacaat	ncggctgaat	ctnaagtctt	gtgttttact	240
aatggaaaaa	aaaaataaac	aanaggtttt	gttctcatgg	ctgccaccg	cagcctggca	300
ctaaaacanc	ccagcgctca	cttctgcttg	ganaaaatatt	ctttgctctt	ttggacatca	360
ggcttgatgg	tatcactgcc	acntttccac	ccagctgggc	ncccttcccc	catntttgtc	420
antganctgg	aaggcctgaa	ncttagtctc	caaaagtctc	ngcccacaag	accggccacc	480
aggggagtc	ntttncagtg	gatctgccaa	anantaccn	tatcatcnnt	gaataaaaag	540
gcccctgaac	ganatgcttc	cancancctt	taagaccat	aatcctngaa	ccatggtgcc	600
cttccggtct	gatecnaaag	gaatgttctt	gggtcccant	ccctcctttg	ttnccttacgt	660
tgtnttgac	cnttgctngn	atnaccaan	tganatcccc	ngaagcacc	tnccctggc	720
atttganttt	cntaaattct	ctgccctacn	nctgaaagca	cnattccctn	ggcncnaaan	780
ggngaactca	agaaggtctn	ngaaaaacca	cncn			814

<210> 37  
 <211> 760  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(760)  
 <223> n = A,T,C or G

<400> 37						
gcatgctgct	cttccctcaa	gttggttctg	ttgccataac	aaccaccata	ggtaaagcgg	60
gcgcagtgtt	cgctgaagg	gttgtagtac	cagcgcgga	tgctctcctt	gcagagtctt	120
gtgtctggca	ggctccacga	atgccctttg	tactgggga	aatggatgcg	ctggagctcg	180
tcnaanccac	tcgtgtattt	ttcacangca	gcctcctccg	aagcntccgg	gcagttgggg	240
gtgtcgtcac	actccactaa	actgtcgatn	cancagccca	ttgctgcagc	ggaactgggt	300
gggctgacag	gtgccagaac	acactggatn	ggcctttcca	tggaagggcc	tgggggaaat	360
cncctnancc	caaactgcct	ctcaaaggcc	accttgccca	ccccgacagg	ctagaaatgc	420
actcttcttc	ccaaaggtag	ttgttcttgt	tgcccaagca	ncctccanca	aaccaaaanc	480
ttgcaaaatc	tgctccgtgg	gggtcatnnn	taccanggtt	ggggaaanaa	acccggcngn	540
ganccnccctt	gtttgaatgc	naaggnaata	atcctcctgt	cttgcttggg	tggaanagca	600
caattgaact	gttaacnttg	ggccgngttc	cncnnggtg	gtctgaaact	aatcaccgtc	660
actgaaaaaa	ggtangtgc	ttccttgaat	tcccaantt	ccctngntt	tgggtntttt	720
ctcctctncc	ctaaaaatcg	tnttcccccc	ccntanggcg			760

18

<210> 38  
 <211> 724  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(724)  
 <223> n = A,T,C or G

<400> 38  
 tttttttttt tttttttttt tttttttttt ttttttaaaaa cccctcccat tgaatgaaaa 60  
 cttccnaaat tgtccaaccc cctcnnccaa atnncattt cggggggggg gttccaaacc 120  
 caaattaatt ttgganttta aattaaatnt tnattngggg aanaanccaa atgtnaagaa 180  
 aatttaaccc attatnaact taaatnccn gaaaccctg gnttccaaaa atttttaacc 240  
 cttaaatccc tccgaaattg ntaanggaaa accaaattcn cctaaggctn tttgaagggt 300  
 ngatttaaac ccccttnant tnttttnacc cnnngnctnaa ntatttngnt tccggtgttt 360  
 tcctnttaan cntnggtaac tcccgnataat gaannnccct aanccaatta aaccgaattt 420  
 tttttgaatt ggaaattccn ngggaattna cgggggtttt tcccnttttg gggccatncc 480  
 cccnctttcg gggtttgggn ntagggtgaa ttttttnang ncccaaaaaa nccccaana 540  
 aaaaaactcc caagnnttaa ttngaantnc ccccttccca ggccttttg gaaaggnggg 600  
 tttntggggg ccngggantt cnttccccn ttncncccc cccccnggt aaanggttat 660  
 ngnttttgtt ttttgggccc cttnanggac cttccggatn gaaattaaat ccccggnncg 720  
 gccg 724

<210> 39  
 <211> 751  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(751)  
 <223> n = A,T,C or G

<400> 39  
 tttttttttt tttttttttg ctcacattta atttttatth tgattttttt taatgctgca 60  
 caacacaata tttatttcat ttgtttcttt tatttcattt tatttgtttg ctgctgctgt 120  
 tttatttatt tttactgaaa gtgagaggga acttttgttg ctttttttcc tttttctgta 180  
 ggccgcctta agctttctaa atttgaaca tctaagcaag ctgaanggaa aaggggggtt 240  
 cgcaaaatca ctgggggaa nggaaagggt gctttgttaa tcatgcccta tgggtgggtga 300  
 ttaactgctt gtacaattac ntctacttt taattaattg tgctnaangc ttttaattana 360  
 cttgggggtt ccctcccan accaaccnccn ctgacaaaaa gtgccngccc tcaaatnatg 420  
 tcccggcnnt cnttgaacaa caengcngaa ngttctcatt ntcccnccn caggtnaaaa 480  
 tgaagggtta ccatntttaa cnccacctcc acntggcnnn gcctgaatcc tcnaaaancn 540  
 ccctcaancn aattnctnng ccccggtcnc gcntnngtcc cncctgggct cggggaantn 600  
 cacccccnga anncnntnnc naacnaaatt ccgaaaatat tcccnntcnc tcaattcccc 660  
 cnnagactnt cctcnnncn cncaattttc tttntntcac gaacncgnnc cnnaaaatgn 720  
 nnnncnctc cntnngtcn naatcnccan c 751

<210> 40  
 <211> 753  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(753)

<223> n = A,T,C or G

<400> 40

gtggtat	ctgtaagatc	agggtgttcct	ccctcgtagg	tttagaggaa	acaccctcat	60
agatgaaaac	ccccccgaga	cagcagcact	gcaactgccca	agcagccggg	gtaggagggg	120
cgccctatgc	acagctgggc	ccttgagaca	gcagggcttc	gatgtcaggc	tcgatgtcaa	180
tggtctggaa	gcgccggctg	tacctgcgta	ggggcacacc	gtcagggccc	accaggaact	240
tctcaaagtt	ccaggcaacn	tcgttgcgac	acaccggaga	ccagggtgatn	agcttgggggt	300
cggtcataa	cggcggtggcg	tcgtcgctgg	gagctggcag	ggcctcccgc	aggaaggcna	360
ataaaaggtg	cgcgcccgca	ccgttcanc	cgcacttctc	naanaccatg	angttgggct	420
cnaaccacc	accannccgg	acttccttga	nggaattccc	aaatctcttc	gntcttgggc	480
ttctnctgat	gccctanctg	gttgcccngn	atgccaanca	nccccaancc	ccgggggtcct	540
aaanaccn	cctctcntt	tcctctgggt	tntntcccc	ggacctgggt	tcctctcaag	600
gganccata	ttctnaccan	tactcacnt	nccccccnt	gnnaccanc	cttctanngn	660
ttcccnccg	ncctctggcc	cntcaaan	gcttnacna	cctgggtctg	ccttcccccc	720
tnccctatct	gnaccn	tttgtctcan	tnt			753

<210> 41

<211> 341

<212> DNA

<213> Homo sapien

<400> 41

actatatcca	tcacaacaga	catgcttcat	cccatagact	tcttgacata	gcttcaaagt	60
agtgaaccca	tccttgattt	atatacatat	atgttctcag	tattttggga	gcctttccac	120
ttctttaaac	cttggttcatt	atgaacactg	aaaataggaa	tttgtgaaga	gttaaaaagt	180
tatagcttgt	ttacgtagta	agtttttgaa	gtctacattc	aatccagaca	cttagttgag	240
tgttaaactg	tgatttttaa	aaaatatcat	ttgagaatat	tctttcagag	gtattttcat	300
ttttactttt	tgatttaattg	tgttttatat	attagggtag	t		341

<210> 42

<211> 101

<212> DNA

<213> Homo sapien

<400> 42

acttactgaa	tttagttctg	tgctcttcct	tatttagtgt	tgtatcataa	atactttgat	60
gtttcaaaca	ttctaaataa	ataattttca	gtggcttcat	a		101

<210> 43

<211> 305

<212> DNA

<213> Homo sapien

<400> 43

acatctttgt	tacagtctaa	gatgtgttct	taaatcacca	ttccttctctg	gtcctcaccc	60
tcagggtgg	tctcacactg	taattagagc	tattgaggag	tctttacagc	aaattaagat	120
tcagatgcct	tgctaagtct	agagttctag	agttatgttt	cagaaagtct	aagaaaccca	180
cctcttgaga	ggtcagtaaa	gaggacttaa	tatttcata	ctacaaaatg	accacaggat	240
tggtacaga	acgagagtta	tcctggataa	ctcagagctg	agtacctgcc	cggggggccgc	300
tcgaa						305

<210> 44

<211> 852

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature  
 <222> (1)...(852)  
 <223> n = A,T,C or G

<400> 44  
 acataaatat cagagaaaag tagtctttga aatattttacg tccaggagtt ctttgtttct 60  
 gattatttgg tgtgtgtttt ggtttgtgtc caaagtattg gcagcttcag ttttcatttt 120  
 ctctccatcc tcgggcattc ttcccaaatt tatataccag tcttcgtcca tccacacgct 180  
 ccagaatttc tctttttag tagtatctca tagctcggct gagcttttca taggtcatgc 240  
 tgctgttgtt cttcttttta ccccatagct gagccactgc ctctgatttc aagaacctga 300  
 agacgccctc agatcgggtc tcccatttta ttaatcctgg gttcttgtct gggttcaaga 360  
 ggatgtcgcg gatgaattcc cataagttag tccctctcgg gttgtgcttt ttgggtgtggc 420  
 acttggcagg ggggtcttgc tcttttttca tatcagggtga ctctgcaaca ggaagggtgac 480  
 tgggtgttgc catggagatc tgagcccgcc agaaagtttt gctgtccaac aaatctactg 540  
 tgctaccata gttgggtgtca tataaatagt tctngtcttt ccagggtgttc atgatggaag 600  
 gctcagtttg ttcagtcttg acaatgacat tgtgtgtgga ctggaacagg tccactactgc 660  
 actggccgtt ccacttcaga tgctgcaagt tgctgtagag gagntgcccc gccgtccctg 720  
 ccgcccgggt gaactcctgc aaactcatgc tgcaaagggt ctcgccgttg atgtcgaact 780  
 cntggaaaag gatacaattg gcatccagct ggttggtgtc caggaggtga tggagccact 840  
 cccacacctg gt 852

<210> 45  
 <211> 234  
 <212> DNA  
 <213> Homo sapien

<400> 45  
 acaacagacc cttgctcgtc aacgacctca tgctcatcaa gttggacgaa tccgtgtccg 60  
 agtctgacac catccggagc atcagcattg cttcgcagtgc cctaccgcg gggaactctt 120  
 gcctcgtttc tggctggggc ctgctggcga acggcagaat gcctaccgtg ctgcagtgcg 180  
 tgaacgtgtc ggtggtgtct gaggaggtct gcagtaagct ctatgaccgc ctgt 234

<210> 46  
 <211> 590  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(590)  
 <223> n = A,T,C or G

<400> 46  
 actttttatt taaatgttta taaggcagat ctatgagaat gatagaaaac atggtgtgta 60  
 atttgatagc aatatttttg agattacaga gttttagtaa ttaccaatta cacagttaaa 120  
 aagaagataa tatattccaa gcanatacaa aatatctaata gaaagatcaa ggcaggaaaa 180  
 tgantataac taattgacaa tggaaaatca attttaattg gaattgcaca ttatccttta 240  
 aaagctttca aaanaanaaa ttattgcagt ctanttaatt caaacagtgt taaatggtat 300  
 caggataaan aactgaaggc canaaagaat taattttcac ttcattgtaac ncaccanatt 360  
 ttacaatggc ttaaatgcan ggaaaaagca gtggaagtag ggaagtantc aaggtctttc 420  
 tggctcttaa tctgccttac tctttgggtg tggctttgat cctctggaga cagctgccag 480  
 ggctcctgtt atatcccaa tcccagcagc aagatgaagg gatgaaaaag gacacatgct 540  
 gccttccttt gaggagactt catctcactg gccaacactc agtcacatgt 590

<210> 47  
 <211> 774  
 <212> DNA  
 <213> Homo sapien

21

<220>  
 <221> misc\_feature  
 <222> (1)...(774)  
 <223> n = A,T,C or G

<400> 47  
 acaagggggc ataatgaagg agtgggggana gatttttaaag aaggaaaaaa aacgaggccc 60  
 tgaacagaat ttctctgnac aacggggcctt caaaataatt ttcttgggga ggttcaagac 120  
 gcttcactgc ttgaaactta aatggatgtg ggacanaatt ttctgtaatg accctgaggg 180  
 cattacagac gggactctgg gaggaaggat aaacagaaag gggacaaaag ctaatcccaa 240  
 aacatcaaag aaaggaaggt ggcgtcatac ctcccagcct acacagttct ccagggtctt 300  
 cctcatccct ggaggacgac agtggaggaa caactgacca tgtcccagg ctctgtgtgtg 360  
 ctgggtctctg gtcttcagcc cccagctctg gaagcccacc ctctgtgat cctgcgtggc 420  
 ccacactcct tgaacacaca tcccaggtt atatttcctgg acatggctga acctcctatt 480  
 cctacttccg agatgccttg ctccctgcag cctgtcaaaa tcccactcac cctccaaacc 540  
 acggcatggg aagcctttct gacttgcctg attactccag catcttgga caatccctga 600  
 ttccccactc cttagaggca agataggggtg gtttaagagta gggctggacc acttgagcc 660  
 aggctgctg cttcaaattn tggtcattt acgagctatg ggaccttggg caagtnatct 720  
 tcacttctat gggontcatt ttgttctacc tgcaaatgg gggataataa tagt 774

<210> 48  
 <211> 124  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(124)  
 <223> n = A,T,C or G

<400> 48  
 canaaattga aattttataa aaaggcattt ttctcttata tccataaaat gatataattt 60  
 ttgcaantat anaaatgtgt cataaattat aatgttcctt aattacagct caacgcaact 120  
 tggt 124

<210> 49  
 <211> 147  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(147)  
 <223> n = A,T,C or G

<400> 49  
 gccgatgcta ctattttatt gcaggaggtg ggggtgtttt tattattctc tcaacagctt 60  
 tgtggctaca ggtggtgtct gactgcatna aaaanttttt tacgggtgat tgcaaaaatt 120  
 ttagggcacc catatcccaa gcantgt 147

<210> 50  
 <211> 107  
 <212> DNA  
 <213> Homo sapien

<400> 50  
 acattaaatt aataaaagga ctgttggggt tctgctaaaa cacatggctt gatatatgtc 60

atggtttgag gttaggagga gttaggcata tgttttggga gaggggt 107

<210> 51  
 <211> 204  
 <212> DNA  
 <213> Homo sapien

<400> 51  
 gtcctaggaa gtctagggga cacacgactc tggggtcacg gggccgacac acttgacagg 60  
 cgggaaggaa aggcagagaa gtgacaccgt cagggggaaa tgacagaaag gaaaatcaag 120  
 gccttgcaag gtcagaaagg ggactcaggg cttccaccac agccctgccc cacttgcca 180  
 cctccctttt gggaccagca atgt 204

<210> 52  
 <211> 491  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(491)  
 <223> n = A,T,C or G

<400> 52  
 acaaagataa catttatctt ataacaaaaa tttgatatgtt ttaaagggtta gtattgtgta 60  
 gggatattttc caaaagacta aagagataac tcaggtaaaa agttagaaat gtataaaaca 120  
 ccatcagaca ggtttttaaa aaacaacata ttacaaaatt agacaatcat ccttaaaaaa 180  
 aaaaacttctt gtatcaattt cttttgttca aaatgactga ctttaantatt tttaaatatt 240  
 tcanaaacac ttctcaaaa attttcaana tggtagcttt canatgtnc ctcagtccca 300  
 atgttgctca gataaataaa tctcgtgaga acttaccacc caccacaagc tttctggggc 360  
 atgcaacagt gtcttttctt tnccttttct ttttttttt ttacaggcac agaaactcat 420  
 caattttatt tggataacaa aggtctcca aattatattg aaaaataaat ccaagttaat 480  
 atcactcttg t 491

<210> 53  
 <211> 484  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(484)  
 <223> n = A,T,C or G

<400> 53  
 acataattta gcagggctaa ttaccataag atgctattta ttaanaggtn tatgatctga 60  
 gtattaacag ttgctgaagt ttggtatttt tatgcagcat tttctttttg ctttgataac 120  
 actacagaac ccttaaggac actgaaaatt agtaagtaaa gttcagaaac attagctgct 180  
 caatcaaact tctacataac actatagtaa ttaaaacggt aaaaaaagt gttgaaatct 240  
 gcactagtat anaccgctcc tgtcaggata anactgcttt ggaacagaaa gggaaaaanc 300  
 agctttgant tttttgtgc tgatangagg aaaggctgaa ttacctgtt gcctctccct 360  
 aatgattggc aggtcnggta aatnccaaaa catattccaa ctcaacactt cttttccncg 420  
 tancctgant ctgtgtattc caggancagg cggatggaat gggccagccc ncggatgttc 480  
 cant 484

<210> 54  
 <211> 151  
 <212> DNA

<213> Homo sapien

<400> 54

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actaaacctc gtgcttgtga actccataca gaaaacggtg ccatacctga acacggctgg      60
ccactgggta tactgctgac aaccgcaaca acaaaaacac aaatccttgg cactggctag      120
tctatgtcct ctcaagtgcc tttttgtttg t                                     151
```

<210> 55

<211> 91

<212> DNA

<213> Homo sapien

<400> 55

```
acctggcttg tctccgggtg gttccggcg cccccacgg tccccagaac ggacactttc      60
gccctccagt ggatactcga gccaaagtgg t                                     91
```

<210> 56

<211> 133

<212> DNA

<213> Homo sapien

<400> 56

```
ggcggatgtg cgttggttat atacaaatat gtcattttat gtaagggact tgagtatact      60
tggatttttg gtatctgtgg gttgggggga cggccagga accaataccc catggatacc      120
aagggacaac tgt                                     133
```

<210> 57

<211> 147

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(147)

<223> n = A,T,C or G

<400> 57

```
actctggaga acctgagccg ctgctccgcc tctgggatga ggtgatgcan gcngtggcgc      60
gactgggagc tgagcccttc cctttgcgcc tgcctcagag gattgttgcc gacntgcana      120
tctcantggg ctggatncat gcagggt                                     147
```

<210> 58

<211> 198

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(198)

<223> n = A,T,C or G

<400> 58

```
acagggatat aggtttinaag ttattgtnat tgtaaaatac attgaatttt ctgtatactc      60
tgattacata catttatcct ttaaaaaaga tgtaaatcct aatttttatg ccatactatta      120
atttaccaat gagttacctt gtaaatgaga agtcatgata gactgaatt ttaactagtt      180
ttgacttcta agtttggt                                     198
```

<210> 59



24

<211> 330  
 <212> DNA  
 <213> Homo sapien

<400> 59  
 acaacaaatg ggttgtagg aagtcttata agcaaaactg gtgatggcta ctgaaaagat 60  
 ccattgaaaa ttatcattaa tgattttaaa tgacaagtta tcaaaaactc actcaatttt 120  
 cacctgtgct agcttgctaa aatgggagtt aactctagag caaatatagt atcttctgaa 180  
 tacagtcaat aaatgacaaa gccaggcct acaggtgggt tccagacttt ccagaccag 240  
 cagaaggaat ctattttatc acatggatct ccgtctgtgc tcaaaatacc taatgatatt 300  
 tttcgtcttt attggacttc tttgaagagt 330

<210> 60  
 <211> 175  
 <212> DNA  
 <213> Homo sapien

<400> 60  
 accgtgggtg ccttctacat tctgaaggc tcttcacca acatctggtt ctacttcggc 60  
 gtcgtgggct ccttcctctt catcctcatc cagctgggtc tgctcatcga ctttgcgac 120  
 tcttgaacc agcggtaggt gggcaaggcc gaggagtgcg attcccgtgc ctggt 175

<210> 61  
 <211> 154  
 <212> DNA  
 <213> Homo sapien

<400> 61  
 accccaactt tctcctgtg agcagtctgg acttctcact gctacatgat gagggtagt 60  
 ggtgtgtgct cttcaacagt atcctcccct ttccggatct gctgagccgg acagcagtgc 120  
 tggactgcac agccccgggg ctccacattg ctgt 154

<210> 62  
 <211> 30  
 <212> DNA  
 <213> Homo sapien

<400> 62  
 cgctcgagcc ctatagttag tcgtattaga 30

<210> 63  
 <211> 89  
 <212> DNA  
 <213> Homo sapien

<400> 63  
 acaagtcatt tcagcacctt ttgctcttca aaactgacca tcttttatat ttaatgcttc 60  
 ctgtatgaat aaaaatgggt atgtcaagt 89

<210> 64  
 <211> 97  
 <212> DNA  
 <213> Homo sapien

<400> 64  
 accggagtaa ctgagtcggg acgctgaatc tgaatccacc aataaataaa ggttctgcag 60  
 aatcagtga tccaggattg gtccttgat ctgggg 97

<210> 65  
 <211> 377  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(377)  
 <223> n = A,T,C or G

<400> 65  
 acaacaanaa ntcccttctt taggccactg atggaaacct ggaacccctt tttgatggca 60  
 gcatggcgctc ctaggccttg acacagcggc tgggggtttg gctntcccaa accgcacacc 120  
 ccaaccctgg tctaccaca nttctggcta tgggctgtct ctgccactga acatcagggg 180  
 tcggtcataa natgaaatcc caanggggac agagggtcagt agaggaagct caatgagaaa 240  
 ggtgctgttt gctcagccag aaaacagctg cctggcattc gccgctgaac tatgaaccgg 300  
 tgggggtgaa ctacccccc gaggaatcat gcctgggcga tgcaanggtg ccaacaggag 360  
 gggcgggagg agcatgt 377

<210> 66  
 <211> 305  
 <212> DNA  
 <213> Homo sapien

<400> 66  
 acgcctttcc ctccagaattc agggaagaga ctgtgcgctg ccttctctcg ttgttgcggtg 60  
 agaaccgggtg tgccccttcc caccatatcc accctcgctc catctttgaa ctcaaacacg 120  
 aggaactaac tgcaccctgg tctctctccc agtccccagt tcaccctcca tccctcacct 180  
 tctccactc taagggatat caacactgcc cagcacaggg gccctgaatt tatgtgggtt 240  
 ttatatattt ttttaataaga tgcactttat gtcatttttt aataaagtct gaagaattac 300  
 tggtt 305

<210> 67  
 <211> 385  
 <212> DNA  
 <213> Homo sapien

<400> 67  
 actacacaca ctccacttgc ctttgtgaga cactttgtcc cagcacttta ggaatgctga 60  
 ggtcggacca gccacatctc atgtgcaaga ttgccagca gacatcaggt ctgagagttc 120  
 cccttttaaa aaaggggact tgcttaaaaa agaagtctag ccacgattgt gtagagcagc 180  
 tgtgtgtgtc tggagattca cttttgagag agttctcctc tgagacctga tctttagagg 240  
 ctgggcagtc ttgcacatga gatggggctg gtctgatctc agcactcctt agtctgcttg 300  
 cctctcccag ggccccagcc tggccacacc tgcttacagg gcaactctcag atgcccatac 360  
 catagtttct gtgctagtgg accgt 385

<210> 68  
 <211> 73  
 <212> DNA  
 <213> Homo sapien

<400> 68  
 acttaaccag atatattttt accccagatg gggatattct ttgtaaaaaa tgaaaataaa 60  
 gtttttttaa tgg 73

<210> 69  
 <211> 536  
 <212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(536)

<223> n = A,T,C or G

<400> 69

actagtccag	tgtggtggaa	ttccattgtg	ttggggggctc	tcaccctcct	ctcctgcagc	60
tccagctttg	tgtctgcct	ctgaggagac	catggcccag	catctgagta	ccctgctgct	120
cctgctggcc	accctagctg	tggccctggc	ctggagcccc	aaggaggagg	ataggataat	180
ccgggtggc	atctataacg	cagacctcaa	tgatgagtgg	gtacagcgtg	cccttcactt	240
cgccatcagc	gagtataaca	aggccaccaa	agatgactac	tacagacgtc	cgctgcgggt	300
actaagagcc	aggcaacaga	ccgttggggg	ggtgaattac	ttcttcgacg	tagaggtggg	360
ccgaaccata	tgtaccaagt	cccagcccaa	cttggacacc	tgtgccttcc	atgaacagcc	420
agaactgcag	aagaaacagt	tgtgctcttt	cgagatctac	gaagttccct	ggggagaaca	480
gaangtccct	gggtgaaatc	caggtgtcaa	gaaatcctan	ggatctgttg	ccaggc	536

<210> 70

<211> 477

<212> DNA

<213> Homo sapien

<400> 70

atgaccccta	acagggggccc	tctcagccct	cctaattgacc	tcgggcctag	ccatgtgatt	60
tcacttccac	tccataacgc	tcctcatact	aggcctaacta	accaacacac	taaccatata	120
ccaatgatgg	cgcgatgtaa	cacgagaaag	cacataccaa	ggccaccaca	caccacctgt	180
ccaaaaaggg	cttcgatacg	ggataatcct	atttattacc	tcagaagttt	ttttcttcgc	240
agggattttt	ctgagccttt	taccactcca	gcctagcccc	taccccccaa	ctaggagggc	300
actggccccc	aacaggcatc	accccgctaa	atcccctaga	agtcccactc	ctaaacacat	360
ccgtattact	cgcatcagga	gtatcaatca	cctgagctca	ccatagtcta	atagaaaaca	420
accgaaacca	aattattcaa	agcactgctt	attacaattt	tactgggtct	ctattttt	477

<210> 71

<211> 533

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(533)

<223> n = A,T,C or G

<400> 71

agagctatag	gtacagtgtg	atctcagctt	tgcaaacaca	ttttctacat	agatagtact	60
aggtattaat	agatatgtaa	agaaagaaat	cacaccatta	ataatggtaa	gattggttta	120
tgtgatttta	gtggtatttt	tggcaccctt	atatatgttt	tccaaacttt	cagcagtgat	180
attattttcca	taacttaaaa	agtgagtgtg	aaaaagaaaa	tctccagcaa	gcattctcatt	240
taaataaaagg	tttgtcatct	ttaaaaatac	agcaatatgt	gacttttttaa	aaaagctgtc	300
aaataggtgt	gaccctaacta	ataattatta	gaaatacatt	taaaaacatc	gagtacatca	360
agtcagtttg	ccttgaaaaa	tatcaaatat	aactcttaga	gaaatgtaca	taaaagaatg	420
cttcgtaatt	ttggagtang	aggttccctc	ctcaattttg	tattttttaa	aagtacatgg	480
taaaaaaaaa	aattcacac	agtatataag	gctgtaaaaa	gaagaattct	gcc	533

<210> 72

<211> 511

<212> DNA

<213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(511)  
 <223> n = A,T,C or G

<400> 72  
 tattacggaa aaacacacca cataattcaa ctancaaaga anactgcttc agggcgtgta 60  
 aaatgaaaagg cttccaggca gttatctgat taaagaacac taaaagaggg acaaggctaa 120  
 aagccgcagg atgtctacac tatancaggc gctatttggg ttggctggag gagctgtgga 180  
 aaacatggan agattggtgc tgganacgc cgtggctatt cctcattgtt attacanagt 240  
 gaggttctct gtgtgccac tggtttgaaa accgttctnc aataatgata gaatagtaca 300  
 cacatgagaa ctgaaatggc ccaaaccag aaagaaagcc caactagatc ctcagaanac 360  
 gcttctaggg acaataaccg atgaagaaaa gatggcctcc ttgtgcccc gtctgttatg 420  
 atttctctcc attgcagcna naaaccggtt cttctaagca aacncagggtg atgatggcna 480  
 aaatacacc cctcttgaag naccnggagg a 511

<210> 73  
 <211> 499  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(499)  
 <223> n = A,T,C or G

<400> 73  
 cagtgccagc actggtgcc a gtaccagtag caataacagt gccagtgcc gtgccagcac 60  
 cagtgggtggc ttcagtgtg gtgccagcct gaccgccact ctcacatttg ggctcttcgc 120  
 tggccttggg ggagctgggt ccagcaccag tggcagctct ggtgcctgtg gtttctccta 180  
 caagttagat tttagatatt gttaatcctg ccagtctttc tcttcaagcc aggggtgcac 240  
 ctcagaaacc tactcaacac agcactctag gcagccaact tcaatcaatt gaagttgaca 300  
 ctctgcatta aatctatttg ccatttctga aaaaaaaaaa aaaaaaagg cgccgctcg 360  
 antctagagg gcccgtttaa acccgctgat cagcctogac tgtgccttct anttgccagc 420  
 catctgttgt ttgccctcc cccgntgcct tccttgacct tggaaagtgc cactcccact 480  
 gtcccttctc aantaaaat 499

<210> 74  
 <211> 537  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(537)  
 <223> n = A,T,C or G

<400> 74  
 tttcatagga gaacacactg aggagatact tgaagaattt ggattcagcc gcgaagagat 60  
 ttatcagctt aactcagata aaatcattga aagtaataag gtaaaagcta gtctctaact 120  
 tocaggccca cggtcaagt gaatttgaat actgcattta cagtgtagag taacacataa 180  
 cattgtatgc atggaaacat ggaggaacag tattacagtg tcctaccact ctaatcaaga 240  
 aaagaattac agactctgat tctacagtga tgattgaatt ctaaaaatgg taatcattag 300  
 ggcttttgat ttataanact ttgggtactt atactaaatt atggtagtta tactgccttc 360  
 cagttgtgctt gatataattg ttgatattaa gattcttgac ttatattttg aatgggttct 420  
 actgaaaaan gaatgatata ttcttgaaga catcgatata catttattta cactcttgat 480  
 tctacaatgt agaaaatgaa ggaaatgccc caaattgtat ggtgataaaa gtcccggt 537

<210> 75  
 <211> 467  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(467)  
 <223> n = A,T,C or G

<400> 75  
 caaanacaat tgttcaaaaag atgcaaataga tacactactg ctgcagctca caaacacctc 60  
 tgcattattac acgtacctcc tcctgctcct caagtagtgt ggtctatattt gccatcatca 120  
 cctgctgtct gcttagaaga acggctttct gctgcaangg agagaaatca taacagacgg 180  
 tggcacaagg aggccatctt ttctcatcgt gttattgtcc ctagaagcgt cttctgagga 240  
 tctagttggg ctttctttct gggtttgggc catttcantt ctcattgtgt tactattcta 300  
 tcattattgt ataacggtt tcaaaccngt gggcacncag agaacctcac tctgtaataa 360  
 caatgaggaa tagccacggg gatctccagc accaaatctc tccatgttnt tccagagctc 420  
 ctocagccaa cccaaatagc cgctgctatn gtgtagaaca tccctgn 467

<210> 76  
 <211> 400  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(400)  
 <223> n = A,T,C or G

<400> 76  
 aagctgacag cattcgggcc gagatgtctc gctccgtggc cttagctgtg ctgcgctac 60  
 tctctcttc tggcctggag gctatccagc gtactccaaa gattcaggtt tactcacgct 120  
 atccagcaga gaatggaag tcaaatttcc tgaattgcta tgtgtctggg ttcatccat 180  
 ccgacattga agttgactta ctgaagaatg gagagagaat tgaaaaagt gagcattcag 240  
 acttgcttt cagcaaggac tggctttct atctcttgta ctacactgaa ttcaccccca 300  
 ctgaaaaaga tgagtatgcc tgccgtgtga accatgtgac tttgtcacag cccaagatng 360  
 ttnagtggga tcganacatg taagcagcan catgggaggt 400

<210> 77  
 <211> 248  
 <212> DNA  
 <213> Homo sapien

<400> 77  
 ctggagtgcc ttggtgtttc aagcccctgc aggaagcaga atgcaccttc tgaggcacct 60  
 ccagctgccc cggcggggga tgcgaggtc ggagcacctc tgcccggctg tgattgtgct 120  
 caggcaactgt tcatctcagc ttttctgtcc ctttgtcacc ggcaagcgct tctgctgaaa 180  
 gttcatatct ggagcctgat gtcttaacga ataaaggctc catgctccac ccgaaaaaaa 240  
 aaaaaaaa 248

<210> 78  
 <211> 201  
 <212> DNA  
 <213> Homo sapien

<400> 78

29

```

actagtccag tgtgggtggaa ttccattgtg ttggggcccaa cacaatggct acctttaaca    60
tcacccagac cccgccctgc cgtgcccga cgctgctgct aacgacagta tgatgcttac    120
tctgctactc ggaaactatt tttatgtaat taatgtatgc tttcttgttt ataatgcct    180
gatttaaaaa aaaaaaaaaa a                                201

```

```

<210> 79
<211> 552
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(552)
<223> n = A,T,C or G

```

```

<400> 79
tccttttgtt aggtttttga gacaacccta gacctaaact gtgtcacaga cttctgaatg    60
tttaggcagt gctagtaatt tcctcgtaat gattctgtta ttactttcct attctttatt    120
cctctttcct ctgaagatta atgaagttga aaattgaggt ggataaatac aaaaaggtag    180
tgtgatagta taagtatcta agtgcagatg aaagtgtgtt atatatatcc attcaaaatt    240
atgcaagtta gtaattactc aggtttaaact aaattacttt aatatgctgt tgaacctact    300
ctgttccttg gctagaaaaa attataaaca ggactttgtt agtttgggaa gccaaattga    360
taatatctta tgtttctaaa gttgggctat acataaanta tnaagaaata tggaatttta    420
ttcccaggaa tatgggggttc atttatgaat antaccggg anagaagttt tgantnaaac    480
cngtttttgt taatacgtta atatgtcctn aatnaacaag gcntgactta tttocaaaaa    540
aaaaaaaaaa aa                                552

```

```

<210> 80
<211> 476
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(476)
<223> n = A,T,C or G

```

```

<400> 80
acaggggattt gagatgctaa ggccccagag atcgtttgat ccaaccctct tattttcaga    60
ggggaaaaatg gggcctagaa gttacagagc atctagctgg tgcgctggca cccctggcct    120
cacacagact ccgagtagc tgggactaca ggcacacagt cactgaagca ggccctgttt    180
gcaattcacg ttgccacctc caacttaaac attcttcata tgtgatgtcc ttagtcacta    240
agggttaaact ttcccaccca gaaaaggcaa cttagataaa atcttagagt actttcatac    300
tcttctaagt cctcttccag cctcactttg agtcctcctt gggggttgat aggaantntc    360
tcttggtttt ctcaataaaa tctctatcca tctcatgttt aatttggtac gntaaaaaat    420
gctgaaaaaa ttaaaatgtt ctgggttcnc tttaaaaaaa aaaaaaaaaa aaaaaa    476

```

```

<210> 81
<211> 232
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(232)
<223> n = A,T,C or G

```

```

<400> 81

```

```

tttttttttg tatgcntcn ctgtgnggtt attgttgctg ccaccttga ggagcccagt      60
ttcttctgta tctttctttt ctgggggata ttcttggtc tgcccctcca ttcccagcct    120
ctcatcccca tcttgcaact ttgttagggg tggaggcgtc ttcttggtag cccctcagag    180
actcagtcag cgggaataag tcctaggggt ggggggtgtg gcaagccggc ct           232

```

```

<210> 82
<211> 383
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(383)
<223> n = A,T,C or G

```

```

<400> 82
aggcgggagc agaagctaaa gccaaagccc aagaagagtg gcagtgccag cactggtgcc      60
agtaccagta ccaataacat gccagtgccg gtgccagcac cagtgtgtggc ttcaagtgtg    120
gtgccagcct gaccgcact ctcacatttg ggctcttcgc tggccttggt ggagctggtg    180
ccagcaccag tggcagctct ggtgcctgtg gtttctcta caagtgagat tttagatatt    240
gttaatcctg ccagtccttc tcttcaagcc aggggtgcac ctcagaaacc tactcaacac    300
agcactctng gcagccacta tcaatcaatt gaagttgaca ctctgcatta aatctatttg    360
ccatttcaaa aaaaaaaaaa aaa           383

```

```

<210> 83
<211> 494
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(494)
<223> n = A,T,C or G

```

```

<400> 83
accgaatttg gaccgctggc ttataagcga tcatgtcttc cagtattacc tcaacgagca      60
gggagatcga gtctatacgc tgaagaaatt tgaccgatg ggacaacaga cctgctcagc    120
ccatcctgct cggttctccc cagatgacaa atactctcga caccgaatca ccatcaagaa    180
acgcttcaag gtgctcatga cccagcaacc gcgccctgtc ctctgagggg ccttaactg    240
atgtcttttc tgccacctgt taccctcgg agactccgta accaaactct tcggactgtg    300
agccctgatg cctttttgcc agccatactc tttggcntcc agtctctcgt ggcgattgat    360
tatgcttggt tgaggcaatc atggtggcat caccatnaa gggaacacat ttganttttt    420
tttncatat tttaaattac naccagaata nttcagaata aatgaattga aaaactotta    480
aaaaaaaaa aaaa           494

```

```

<210> 84
<211> 380
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(380)
<223> n = A,T,C or G

```

```

<400> 84
gctggtagcc tatggcgtgg ccacggangg gctcctgagg cacgggacag tgacttccca      60
agtatcctgc gccgcgtctt ctaccgtccc tacctgcaga tcttcgggca gattccccag    120

```

```

gaggacatgg acgtggccct catggagcac agcaactgct cgtcggagcc cggtttctgg 180
gcacaccctc ctggggccca ggcgggcacc tgcgtotccc agtatgcca ctggctgggtg 240
gtgctgctcc tcgtcatctt cctgctcgtg gccaacatcc tgcctggtcac ttgctcattg 300
ccatgttcag ttacacattc ggcaaagtac agggcaacag cnatctctac tgggaaggcc 360
agcgttnccg cctcatccgg 380

```

```

<210> 85
<211> 481
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(481)
<223> n = A,T,C or G

```

```

<400> 85
gagttagctc ctccacaacc ttgatgaggt cgtctgcagt ggcctctcgc ttcataccgc 60
tnccatcgct atactgtagg tttgccacca cctcctgcat cttggggcgg ctaatatcca 120
ggaaactctc aatcaagtca ccgtcnatna aacctgtggc tggttctgtc ttccgctcgg 180
tgtgaaagga tctccagaag gagtgctcga tcttccccac acttttgatg actttattga 240
gtcgattctg catgtccagc aggaggttgt accagctctc tgacagtgag gtcaccagcc 300
ctatcatgcc nttgaacgtg ccgaagaaca ccgagccttg tgtggggggg gnagtctcac 360
ccagattctg cattaccaga nagcogtggc aaaaganatt gacaactcgc ccaggngaa 420
aaagaacacc tcctggaagt gctngccgct cctcgtcctt tggtggnngc gcntnccttt 480
t 481

```

```

<210> 86
<211> 472
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(472)
<223> n = A,T,C or G

```

```

<400> 86
aacatcttcc tgtataatgc tgtgtaatat cgatccgatn ttgtotgctg agaattcatt 60
acttggaana gcaacttnaa gcctggacac tggattataa attcacaata tgcaacactt 120
taaacagtgt gtcaatctgc tcccttactt tgtcatcacc agtctgggaa taagggtatg 180
ccctattcac acctgttaaa agggcgctaa gcatttttga ttcaacatct ttttttttga 240
cacaagtccg aaaaaagcaa aagtaaacag ttnttaattt gttagccaat tcactttctt 300
catgggacag agccatttga tttaaaaagc aaattgcata atattgagct ttgggagctg 360
atatntgagc ggaagantag cttttctact tcaccagaca caactccttt catattggga 420
tgttnacnaa agttatgtct cttacagatg ggatgctttt gtggcaattc tg 472

```

```

<210> 87
<211> 413
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(413)
<223> n = A,T,C or G

```

```

<400> 87

```



```

agaaccagtg atctctnaaa acaacctctc ataccttggt gacctaatgt tgtgtgcgtg      60
tgtgtgtgcg cgcatattat atagacaggc acatcttttt tacttttgta aaagcttatg      120
cctcttttgt atctatatct gtgaaagttt taatgatctg ccataatgtc ttggggacct      180
ttgtcttctg tgtaaaggtg actagagaaa acacctatnt tatgagtcaa tctagttngt      240
tttattcgac atgaaggaaa tttccagatn acaacactna caaactctcc cttgactagg      300
ggggacaaaag aaaagcanaa ctgaacatna gaaacaattn cctggtgaga aatnccataa      360
acagaaattg ggtngtatat tgaaanangn catcattnaa acgttttttt ttt              413

```

```

<210> 88
<211> 448
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(448)
<223> n = A,T,C or G

```

```

<400> 88
cgcagcgggt cctctctatc tagctccagc ctctcgccgt ccccaactcc cgcgtcccgc      60
gtcctagccn accatggccg ggccccgtcg cgccccgtcg ctctgtctgg ccacccctggc      120
cgtggccctg gccgtgagcc ccgcggccgg ctccagtcoc ggcaagccgc cgcgcctggt      180
gggaggccca tggaccccg cgtgaagaag aaggtgtgct gcgtgcactg gactttgccg      240
tcggcnanta caacaaaccc gcaacnactt ttaccnagcn cgcgtgcagc gttgtgccgc      300
cccaancaaa ttgttactng gggtaanata ttcttggaag ttgaacctgg gccaaacnng      360
ttaccagaa ccnagccaat tngaacaatt ncccctccat aacagcccct tttaaaaagg      420
gaancantcc tgnctctttc caaat      448

```

```

<210> 89
<211> 463
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(463)
<223> n = A,T,C or G

```

```

<400> 89
gaattttgtg cactggccac tgtgatggaa ccattgggccc aggatgcttt gagtttatca      60
gtagtgattc tgccaaagtt ggtgttgtaa catgagtatg taaaatgtca aaaaattagc      120
agaggtctag gtctgcatat cagcagacag ttgtgccgtg tattttgtag ccttgaagtt      180
ctcagtgaca agttnnttct gatgcgaagt tctnattcca gtgttttagt cctttgcac      240
tttnatgtn agacttgccct ctntnaaatt gcttttgtnt tctgcaggta ctatctgtgg      300
ttaacaaaa tagaannact tctctgcttn gaanatttga atatcttaca tctnaaaatn      360
aattctctcc ccatannaaa acccangccc ttggganaat ttgaaaaang gntccttcnn      420
aattcnnana anttcagntn tcatacaaca naacngganc ccc              463

```

```

<210> 90
<211> 400
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(400)
<223> n = A,T,C or G

```

```

<400> 90
agggattgaa ggtctnttnt actgtcggac tgttcancca ccaactctac aagttgctgt      60
cttccactca ctgtctgtaa gcntnttaac ccagactgta tcttcataaa tagaacaat      120
tcttcaccag tcacatcttc taggaccttt ttggattcag ttagtataag ctcttccact      180
tccttttgta agacttcac tcgttaaagtc ttaagttttg tagaaaggaa ttttaattgct      240
cgttctctaa caatgtcctc tccttgaagt atttggtgta acaaccacc tnaagtccct      300
ttgtgcatcc attttaaata tacttaatag ggcattggtg cactagggtta aattctgcaa      360
gagtcactctg tctgcaaaag ttgcgttagt atatctgcc      400

```

```

<210> 91
<211> 480
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(480)
<223> n = A,T,C or G

```

```

<400> 91
gagctcggat ccaataatct ttgtctgagg gcagcacaca tatncagtgc catggnaact      60
ggtctacccc acatgggagc agcatgccgt agntatataa ggtcattccc tgagtcagac      120
atgcctcttt gactaccgtg tgccagtgtc ggtgattctc acacacctcc nnccgctctt      180
tgtggaaaaa ctggcacttg nctggaaact gcaagacatc acttacaaat tcacccacga      240
gacacttgaa aggtgtaaca aagcgactct tgcattgctt tttgtccctc cggcaccagt      300
tgtcaatact aaccgcgtgg tttgcctcca tcacatttgt gatctgtagc tctggataca      360
tctcctgaca gtactgaaga acttcttctt ttgtttcaaa agcaactctt ggtgcctgtt      420
ngatcagggt cccatttccc agtcogaatg ttcacatggc atatnttact tcccacaaaa      480

```

```

<210> 92
<211> 477
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(477)
<223> n = A,T,C or G

```

```

<400> 92
atacagccca natcccacca cgaagatgag cttgttgact gagaacctga tgcggtcact      60
ggtcccgtg tagccccagc gactctccac ctgctggaag cggttgatgc tgcactcctt      120
cccacgcagg cagcagcggg gccggtaat gaactccact cgtggcttgg ggttgacggt      180
taantgcagg aagaggctga ccacctcgcg gtocaccagg atgcccgaact gtgcgggacc      240
tgcagcgaaa ctctcgatg gtcattgagc ggaagcgaat gangcccagg gccttgccca      300
gaaccttccg cctgttctct ggcgctacac gcagctgctg ccgctnacac tcggcctcgg      360
accagcggac aaacggcggt gaacagccgc acctcacgga tgcccantgt gtcgcgtctc      420
aggaacggcn ccagcgtgtc caggtcaatg tcgggtgaanc ctccgcgggt aatggcg      477

```

```

<210> 93
<211> 377
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(377)
<223> n = A,T,C or G

```

<400> 93  
gaacggctgg accttgccgc gcattgtgct gctggcagga ataccttggc aagcagctcc 60  
agtcagagca gcccagacc gctgccgccc gaagctaagc ctgcctctgg ccttcccctc 120  
cgccccaatg cagaaccant agtgggagca ctgtgttttag agttaagagt gaacactgtn 180  
tgattttact tgggaatttc ctctgttata tagcttttcc caatgctaata ttccaaacaa 240  
caacaacaaa ataacatggt tgcctgttna gttgtataaa agtangtgat tctgtatnta 300  
aagaaaatat tactgttaca tatactgctt gcaanttctg tattttattgg tncctctggaa 360  
ataaatatat tattaata 377

<210> 94  
<211> 495  
<212> DNA  
<213> Homo sapien  
<220>  
<221> misc\_feature  
<222> (1)...(495)  
<223> n = A,T,C or G

<400> 94  
ccctttgagg ggttaggggc cagttcccag tggaagaaac aggccaggag aantgctgctc 60  
cgagctgang cagatttccc acagtgaccc cagagccctg ggctatagtc tctgaccctc 120  
ccaaggaaaag accaccttct ggggacatgg gctggagggc aggacctaga ggcaccaagg 180  
gaaggcccca ttccggggct gttcccagag gaggaaggga aggggctctg tgtgcccccc 240  
acgaggaana ggccttgant cctgggatca nacaccctt cactgtatc cccacacaaa 300  
tgcaagctca ccaaggtccc ctctcagtc cttccctaca ccctgaacgg nactggccc 360  
acaccacccc agancancca cccgccatgg ggaatgtncct caaggaaatcg cngggcaacg 420  
tggaactctng tcccnnaagg gggcagaatc tccaatagan gganngaacc cttgctnana 480  
aaaaaaaaana aaaaa 495

<210> 95  
<211> 472  
<212> DNA  
<213> Homo sapien  
<220>  
<221> misc\_feature  
<222> (1)...(472)  
<223> n = A,T,C or G

<400> 95  
ggttacttgg ttccattgcc accacttagt ggatgtcatt tagaaccatt ttgtctgctc 60  
cctctggaag ccttgccgag agcggacttt gtaattgttg gagaataact gctgaatttt 120  
tagctgtttt gatttgattc gcaccactgc accacaactc aatatgaaaa ctatttnact 180  
tattttattat cttgtgaaaa gtatacaatg aaaattttgt tcatactgta tttatcaagt 240  
atgatgaaaa gcaatagata tatattcttt tattatgtnn aattatgatt gccattatta 300  
atcggaacaaa tgtggagtgt atgttctttt cacagtaata tatgcctttt gtaacttcac 360  
ttgggttattt tattgtaaat gaattacaaa attcttaatt taagaaaatg gtangttata 420  
tttanttcan taatttcttt cttgtttac gtttaattttg aaaagaatgc at 472

<210> 96  
<211> 476  
<212> DNA  
<213> Homo sapien  
<220>  
<221> misc\_feature

35

&lt;222&gt; (1)...(476)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 96

ctgaagcatt	tcttcaaact	tntctacttt	tgtcattgat	acctgtagta	agttgacaat	60
gtgggtgaaat	ttcaaaaatta	tatgtaactt	ctactagttt	tactttctcc	cccaagtctt	120
ttttaactca	tgatttttac	acacacaatc	cagaacttat	tatatagcct	ctaagtcttt	180
attcttcaca	gtagatgatg	aaagagtcct	ccagtgtctt	gngcanaatg	ttctagntat	240
agctggatac	atacngtggg	agttctataa	actcatacct	cagtgggact	naaccaaaat	300
tgtgttagtc	tcaattccta	ccacactgag	ggagcctccc	aaatcactat	attcttatct	360
gcaggctactc	ctccagaaaa	acngacaggg	caggcttgca	tgaaaaagtn	acatctgcgt	420
tacaaagtct	atcttctctca	nangtctgtn	aaggaacaat	ttaatcttct	agcttt	476

&lt;210&gt; 97

&lt;211&gt; 479

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(479)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 97

actcttttcta	atgctgatat	gatcttgagt	ataagaatgc	atatgtcact	agaatggata	60
aaataatgct	gcaaacttaa	tggtcttatg	caaaatggaa	cgctaataaa	acacagctta	120
caatcgcaaa	tcaaaaactca	caagtgtctca	tctgtttagt	atttagtgta	ataagactta	180
gattgtgctc	cttcggatat	gattgtttct	canatcttgg	gcaatnttcc	ttagtcaaat	240
caggctacta	gaattctggt	attggatatn	tgagagcatg	aaatttttaa	naatacactt	300
gtgattatna	aattaatcac	aaatttcact	tatacctgct	atcagcagct	agaaaaacat	360
ntnnttttta	natcaaagta	ttttgtgttt	ggaantgttn	aaatgaaatc	tgaatgtggg	420
ttcnatctta	ttttttcccn	gacnactant	tnctttttta	gggnctattc	tganccatc	479

&lt;210&gt; 98

&lt;211&gt; 461

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 98

agtgacttgt	cctccaacaa	aaccccttga	tcaagtttgt	ggcactgaca	atcagaccta	60
tgctagtctc	tgctcatctat	tcgctactaa	atgcagactg	gaggggacca	aaaaggggca	120
tcaactccag	ctggattatt	ttggagcctg	caaactctatt	cctacttgta	cggactttga	180
agtgattcag	tttccctctac	ggatgagaga	ctggctcaag	aatatcctca	tgcagcttta	240
tgaagccact	ctgaacacgc	tggttatcta	gatgagaaca	gagaaataaa	gtcagaaaat	300
ttacctggag	aaaagaggct	ttggctgggg	accatcccat	tgaaccttct	cttaaggact	360
ttaagaaaaa	ctaccacatg	ttgtgtatcc	tggtgccggc	cgtttatgaa	ctgaccaccc	420
tttggaataa	tcttgacgct	cctgaacttg	ctcctctgcg	a		461

&lt;210&gt; 99

&lt;211&gt; 171

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 99

gtggcgcgc	gcagggtgtt	cctcgtaccg	cagggccccc	tcccttcccc	aggcgtccct	60
cggcgcctct	gcgggcccga	ggaggagcgg	ctggcgggtg	gggggagtgt	gaccacacct	120
cgggtgagaaa	agccttctct	agcgatctga	gaggcgtgcc	ttgggggtac	c	171

<210> 100  
 <211> 269  
 <212> DNA  
 <213> Homo sapien

<400> 100  
 cgcccgcaag tgcaactcca gctggggccg tgcggaogaa gattctgcca gcagttggtc 60  
 cgactgagac gacggcgccg gcgacagtcg caggtgcagc gcggggccct ggggtcttgc 120  
 aaggctgagc tgacgcccga gaggtcgtgt cacgtcccac gaccttgacg ccgtcgggga 180  
 cagccggaac agagcccggg gaagcgggag gcctcgggga gccctcggg aagggcggcc 240  
 cgagagatac gcaggtgcag gtggccgcc 269

<210> 101  
 <211> 405  
 <212> DNA  
 <213> Homo sapien

<400> 101  
 tttttttttt ttttggaaac tactgagagc acagcaggtc agcaacaagt ttatttttga 60  
 gctagcaagg taacagggta gggcatgggt acatgttcag gtcaacttcc tttgtcgtgg 120  
 ttgattgggt tgtctttatg gggcgggggt ggggtagggg aaacgaagca aataacatgg 180  
 agtgggtgca ccctccctgt agaacctggg tacaagcctt ggggcagttc acctggtctg 240  
 tgaccgtcat tttcttgaca tcaatgttat tagaagtcag gatattcttt agagagtcca 300  
 ctgtttctgga gggagattag ggtttcttgc caaatccaac aaaatccact gaaaaagtgt 360  
 gatgatcagt acgaataacc aggcatattc tcatatcggg ggcca 405

<210> 102  
 <211> 470  
 <212> DNA  
 <213> Homo sapien

<400> 102  
 tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 60  
 ggcactttaat ccattttttat ttcaaaatgt ctacaaattt aatcccatta tacggtattt 120  
 tcaaaatcta aattatttcaa attagccaaa tccttaccaa ataataccca aaaatcaaaa 180  
 atatacttct ttcagcaaac ttgttacata aattaaaaaa atatatacgg ctggtgtttt 240  
 caaagtacaa ttatcttaac actgcaaaaca ttttaaggaa ctaaaataaa aaaaaaact 300  
 ccgcaaaagg taaagggaac aacaaattct tttacaacac cattataaaa atcatatctc 360  
 aaatcttagg ggaatatata cttcacacgg gatcttaact tttactcact ttgtttattt 420  
 ttttaaacca ttgtttgggc ccaacacaat ggaatcccc ctggactagt 470

<210> 103  
 <211> 581  
 <212> DNA  
 <213> Homo sapien

<400> 103  
 tttttttttt ttttttttga ccccccctctt ataaaaaaca agttaccatt ttatttttact 60  
 tacacatatt tattttataa ttggtatttag atattcaaaa ggcagctttt aaaatcaaac 120  
 taaatggaaa ctgccttaga tacataattc ttagggaatta gcttaaaatc tgccataaagt 180  
 gaaaatcttc tctagctctt ttgactgtaa atttttgact cttgtaaaac atccaaattc 240  
 atttttcttg tctttaaaat tatctaattc ttccattttt tccctattcc aagtcaattt 300  
 gcttctctag cctcatttcc tagctottat ctactattag taagtggctt ttttcctaaa 360  
 agggaaaaca ggaagagaaa tggcacacaa aacaaacatt ttatattcat atttctacct 420  
 acgttaataa aatagcattt tgtgaagcca gctcaaaaga aggcttagat ccttttatgt 480  
 ccatttttagt cactaaacga tatcaaagtg ccagaatgca aaaggtttgt gaacatttat 540  
 tcaaaagcta atataagata tttcacatac tcatctttct g 581

<210> 104  
 <211> 578  
 <212> DNA  
 <213> Homo sapien

<400> 104  
 tttttttttt tttttttttt ttttttctctt cttttttttt gaaatgagga tcgagttttt 60  
 cactctctag atagggcatg aagaaaactc atctttccag ctttaaaata acaatcaaatt 120  
 ctcttatgct atatcatatt ttaagttaaa ctaatgagtc actggcttat cttctcctga 180  
 aggaaatctg ttcattcttc tcattcatat agttatatca agtactacct tgcattattga 240  
 gaggtttttc ttctctattt acacatatat ttccatgtga atttgtatca aacctttatt 300  
 ttcattgcaaa ctagaaaata atgtttcttt tgcataagag aagagaacaa tatagcatta 360  
 caaaactgct caaattgttt gttaagttat ccattataat tagttggcag gagctaatac 420  
 aaatcacatt tacgacagca ataataaac tgaagtacca gttaaataatc caaaataatt 480  
 aaaggaacat ttttagcctg ggtataatta gctaattcac tttacaagca tttattagaa 540  
 tgaattcaca tggtattatt cctagcccaa cacaatgg 578

<210> 105  
 <211> 538  
 <212> DNA  
 <213> Homo sapien

<400> 105  
 tttttttttt tttttcagta ataatcagaa caatattttat ttttatattt aaaattcata 60  
 gaaaagtgcc ttacatttaa taaaagtttg tttctcaaag tgatcagagg aattagatat 120  
 gtcttgaaca ccaatattaa tttgaggaaa atacacccaa atacattaag taaattattt 180  
 aagatcatag agcttgtaag tgaaaagata aaatttgacc tcagaaactc tgagcattaa 240  
 aaatccacta ttagcaaaata aattactatg gacttcttgc ttttaattttg tgatgaatat 300  
 ggggtgtcac tggtaaacca acacattctg aaggatacat tacttagtga tagattctta 360  
 tgtactttgc taatacgtgg atatgagttg acaagtttct ctttcttcaa tcttttaagg 420  
 ggcgagaaat gaggaagaaa agaaaaggat tacgcatact gttctttcta tggaaggatt 480  
 agatatgttt cctttgccaa tattaataaaa ataataatgt ttactactag tgaaaccc 538

<210> 106  
 <211> 473  
 <212> DNA  
 <213> Homo sapien

<400> 106  
 tttttttttt ttttttagtc aagtttctat ttttattata attaaagtct tggtcatttc 60  
 atttattagc tctgcaactt acatatttaa attaaagaaa cgtttttagac aactgtacaa 120  
 tttataaatg taagggtgcca ttattgagta atatattcct ccaagagtgg atgtgtccct 180  
 tctccacca actaatgaac agcaacatta gttaattttt attagtagat atacactgct 240  
 gcaaacgcta attctcttct ccatcccat gtgatattgt gtatatgtgt gagttggtag 300  
 aatgcatcac aatctacaat caacagcaag atgaagctag gctgggcttt cggtgaaaat 360  
 agactgtgtc tgtctgaatc aaatgatctg acctatcctc ggtggcaaga actcttcgaa 420  
 ccgcttcctc aaaggcgctg ccacatttgt ggctctttgc acttgtttca aaa 473

<210> 107  
 <211> 1621  
 <212> DNA  
 <213> Homo sapien

<400> 107  
 cgccatggca ctgcagggca tctcggcat ggagctgtcc ggcctggccc cgggcccgtt 60  
 ctgtgctatg gtcctggctg acttcggggc gcgtgtggtg cgcgtggacc ggcccggtc 120  
 ccgctacgag gtgagccgct tgggccgggg caagcgctcg ctagtgtgtg acctgaagca 180  
 gccgcgggga gccgccgtgc tgcggcgctc gtgcaagcgg tcggatgtgc tgctggagcc 240

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cttccgccgc ggtgtcatgg agaaactcca gctgggccca gagattctgc agcgggaaaa 300
tccaaggcctt atttatgcca ggctgagtggt atttggccag tcaggaagct tctgccggtt 360
agctggccac gatatcaact atttggcttt gtcaggtgtt ctctcaaaaa ttggcagaag 420
tggtgagaat ccgtatgccc cgctgaatct cctggctgac tttgctggtg gtggccttat 480
gtgtgcactg ggcattataa tggctctttt tgaccgcaca cgactgaca agggtcaggt 540
cattgatgca aatatgggtg aaggaacagc atatttaagt tcttttctgt ggaaaactca 600
gaaatcgagt ctgtgggaag cacctcgagg acagaacatg ttggatggtg gagcaccttt 660
ctatacgact tacaggacag cagatgggga attcatggct gttggagcaa tagaacccca 720
gtttacagag ctgctgatca aaggacttgg actaaagtct gatgaacttc ccaatcagat 780
gagcatggat gattggccag aaatgaagaa gaagtttgca gatgtatttg caaagaagac 840
gaaggcagag tgggtgcaaa tctttgacgg cacagatgcc tgtgtgactc cggttctgac 900
ttttgaggag gttgttcac atgacacaa caaggaacgg ggctcgttta tcaccagtga 960
ggagcaggag gtgagcccc gccctgcacc tctgtgttta aacaccccag ccatcccttc 1020
tttcaaaagg gatcctttca taggagaaca cactgaggag atacttgaag aatttggatt 1080
cagccgcgaa gagatttacc agcttaactc agataaaatc attgaaagta ataaggtaaa 1140
agctagtctc taacttcag gccacggct caagtgaatt tgaatactgc atttacagt 1200
tagagtaaca cataacattg tatgcatgga aacatggagg aacagtatta cagtgtccta 1260
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aatggttatc attagggtt ttgatttata aaactttggg tacttatact aaattatggt 1380
agttattctg ccttcagtt tgcttgatat atttggatg attaagattc ttgacttata 1440
ttttgaatgg gttctagtga aaaaggaatg atatatctt gaagacatcg atatacat 1500
atttacactc ttgattctac aatgtagaaa atgaggaaat gccacaaatt gtatgggtgat 1560
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a

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<210> 108
<211> 382
<212> PRT
<213> Homo sapien

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<400> 108
Met Ala Leu Gln Gly Ile Ser Val Met Glu Leu Ser Gly Leu Ala Pro
1 5 10 15
Gly Pro Phe Cys Ala Met Val Leu Ala Asp Phe Gly Ala Arg Val Val
20 25 30
Arg Val Asp Arg Pro Gly Ser Arg Tyr Asp Val Ser Arg Leu Gly Arg
35 40 45
Gly Lys Arg Ser Leu Val Leu Asp Leu Lys Gln Pro Arg Gly Ala Ala
50 55 60
Val Leu Arg Arg Leu Cys Lys Arg Ser Asp Val Leu Leu Glu Pro Phe
65 70 75 80
Arg Arg Gly Val Met Glu Lys Leu Gln Leu Gly Pro Glu Ile Leu Gln
85 90 95
Arg Glu Asn Pro Arg Leu Ile Tyr Ala Arg Leu Ser Gly Phe Gly Gln
100 105 110
Ser Gly Ser Phe Cys Arg Leu Ala Gly His Asp Ile Asn Tyr Leu Ala
115 120 125
Leu Ser Gly Val Leu Ser Lys Ile Gly Arg Ser Gly Glu Asn Pro Tyr
130 135 140
Ala Pro Leu Asn Leu Leu Ala Asp Phe Ala Gly Gly Gly Leu Met Cys
145 150 155 160
Ala Leu Gly Ile Ile Met Ala Leu Phe Asp Arg Thr Arg Thr Asp Lys
165 170 175
Gly Gln Val Ile Asp Ala Asn Met Val Glu Gly Thr Ala Tyr Leu Ser
180 185 190
Ser Phe Leu Trp Lys Thr Gln Lys Ser Ser Leu Trp Glu Ala Pro Arg
195 200 205
Gly Gln Asn Met Leu Asp Gly Gly Ala Pro Phe Tyr Thr Thr Tyr Arg

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210	215	220
Thr Ala Asp Gly Glu Phe Met Ala Val Gly Ala Ile Glu Pro Gln Phe		
225	230	235
Tyr Glu Leu Leu Ile Lys Gly Leu Gly Leu Lys Ser Asp Glu Leu Pro		
	245	250
Asn Gln Met Ser Met Asp Asp Trp Pro Glu Met Lys Lys Lys Phe Ala		
	260	265
Asp Val Phe Ala Lys Lys Thr Lys Ala Glu Trp Cys Gln Ile Phe Asp		
	275	280
Gly Thr Asp Ala Cys Val Thr Pro Val Leu Thr Phe Glu Glu Val Val		
	290	295
His His Asp His Asn Lys Glu Arg Gly Ser Phe Ile Thr Ser Glu Glu		
305	310	315
Gln Asp Val Ser Pro Arg Pro Ala Pro Leu Leu Leu Asn Thr Pro Ala		
	325	330
Ile Pro Ser Phe Lys Arg Asp Pro Phe Ile Gly Glu His Thr Glu Glu		
	340	345
Ile Leu Glu Glu Phe Gly Phe Ser Arg Glu Glu Ile Tyr Gln Leu Asn		
	355	360
Ser Asp Lys Ile Ile Glu Ser Asn Lys Val Lys Ala Ser Leu		
370	375	380

&lt;210&gt; 109

&lt;211&gt; 1524

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 109

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&lt;210&gt; 110

&lt;211&gt; 3410

&lt;212&gt; DNA



&lt;213&gt; Homo sapien

&lt;400&gt; 110

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gaggtcttat	ctctcagggg	gggttttaagt	gccgttttga	ataatgtcgt	cttattttatt	3240
tagcgggggtg	aatatttttat	actgtaagtg	agcaatcaga	gtataatgtt	tatgggtgaca	3300

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 aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaataa aaaaaaaaaa 3410

<210> 111  
 <211> 1289  
 <212> DNA  
 <213> Homo sapien

<400> 111  
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 ccattgcagt cttcagcttc attaaagacca tgatgatcct cttcaatttg ctcatctttc 180  
 tgtgtggtgc agccctgttg gcagtgggca tctgggtgtc aatcgatggg gcaccccttc 240  
 tgaagatctt cgggccactg tcgtccagtg ccatgcagtt tgtcaacgtg ggctacttcc 300  
 tcatcgcagc cggcgttgtg gtctttgtct ttgggttctt gggtgctat ggtgctaaga 360  
 ctgagagcaa gtgtgccctc gtgacgttct tcttcacctc cctcctcatc ttcatgtctg 420  
 aggttgacgc tgctgtggtc gccttggtgt acaccacaat ggctgagcac ttctgacgt 480  
 tgctggtagt gcctgccatc aagaaagatt atggttccca ggaagacttc actcaagtgt 540  
 ggaacaccac catgaaaggc ctcaagtgtc gtggcttcac caactatacg gattttgagg 600  
 actcacccta cttcaaagag aacagtgcct ttccccatt ctgttgcaat gacaacgtca 660  
 ccaacacagc caatgaaacc tgcaccaagc aaaaggetca cgaccaaaaa gtagagggtt 720  
 gcttcaatca gcttttgtat gacatccgaa ctaatgcagt caccgtgggt ggtgtggcag 780  
 ctggaattgg gggcctcgag ctggctgccca tgattgtgtc catgtatctg tactgcaatc 840  
 tacaataagt ccacttctgc ctotgccact actgtgccca catgggaact gtgaagaggc 900  
 accctggcaa gcagcagtga ttgggggagg ggacaggatc taacaatgtc acttgggcca 960  
 gaatggacct gccctttctg ctocagactt ggggctagat agggaccact ccttttagcg 1020  
 atgcctgact ttccttccat tgggtgggtg atgggtgggg ggcattccag agcctctaag 1080  
 gtagccagtt ctgttgccca ttccccagt ctattaaacc cttgatatgc cccctaggcc 1140  
 tagtggtgat ccagtgctc tactggggga tgagagaaag gcattttata gcctgggcat 1200  
 aagtgaatc agcagagcct ctgggtggat gtgtagaagg cacttcaaaa tgcataaacc 1260  
 tgttacaatg ttaaaaaaaaa aaaaaaaaaa 1289

<210> 112  
 <211> 315  
 <212> PRT  
 <213> Homo sapien

<400> 112  
 Met Val Phe Thr Val Arg Leu Leu His Ile Phe Thr Val Asn Lys Gln  
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 Leu Gly Pro Lys Ile Val Ile Val Ser Lys Met Met Lys Asp Val Phe  
 20 25 30  
 Phe Phe Leu Phe Phe Leu Gly Val Trp Leu Val Ala Tyr Gly Val Ala  
 35 40 45  
 Thr Glu Gly Leu Leu Arg Pro Arg Asp Ser Asp Phe Pro Ser Ile Leu  
 50 55 60  
 Arg Arg Val Phe Tyr Arg Pro Tyr Leu Gln Ile Phe Gly Gln Ile Pro  
 65 70 75 80  
 Gln Glu Asp Met Asp Val Ala Leu Met Glu His Ser Asn Cys Ser Ser  
 85 90 95  
 Glu Pro Gly Phe Trp Ala His Pro Pro Gly Ala Gln Ala Gly Thr Cys  
 100 105 110  
 Val Ser Gln Tyr Ala Asn Trp Leu Val Val Leu Leu Leu Val Ile Phe  
 115 120 125  
 Leu Leu Val Ala Asn Ile Leu Leu Val Asn Leu Leu Ile Ala Met Phe  
 130 135 140  
 Ser Tyr Thr Phe Gly Lys Val Gln Gly Asn Ser Asp Leu Tyr Trp Lys  
 145 150 155 160

Ala Gln Arg Tyr Arg Leu Ile Arg Glu Phe His Ser Arg Pro Ala Leu  
 165 170 175  
 Ala Pro Pro Phe Ile Val Ile Ser His Leu Arg Leu Leu Leu Arg Gln  
 180 185 190  
 Leu Cys Arg Arg Pro Arg Ser Pro Gln Pro Ser Ser Pro Ala Leu Glu  
 195 200 205  
 His Phe Arg Val Tyr Leu Ser Lys Glu Ala Glu Arg Lys Leu Leu Thr  
 210 215 220  
 Trp Glu Ser Val His Lys Glu Asn Phe Leu Leu Ala Arg Ala Arg Asp  
 225 230 235 240  
 Lys Arg Glu Ser Asp Ser Glu Arg Leu Lys Arg Thr Ser Gln Lys Val  
 245 250 255  
 Asp Leu Ala Leu Lys Gln Leu Gly His Ile Arg Glu Tyr Glu Gln Arg  
 260 265 270  
 Leu Lys Val Leu Glu Arg Glu Val Gln Gln Cys Ser Arg Val Leu Gly  
 275 280 285  
 Trp Val Ala Glu Ala Leu Ser Arg Ser Ala Leu Leu Pro Pro Gly Gly  
 290 295 300  
 Pro Pro Pro Pro Asp Leu Pro Gly Ser Lys Asp  
 305 310 315

<210> 113  
 <211> 553  
 <212> PRT  
 <213> Homo sapien

<400> 113  
 Met Val Gln Arg Leu Trp Val Ser Arg Leu Leu Arg His Arg Lys Ala  
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 20 25 30  
 Ala Ala Gly Ile Thr Tyr Val Pro Leu Leu Leu Glu Val Gly Val  
 35 40 45  
 Glu Glu Lys Phe Met Thr Met Val Leu Gly Ile Gly Pro Val Leu Gly  
 50 55 60  
 Leu Val Cys Val Pro Leu Leu Gly Ser Ala Ser Asp His Trp Arg Gly  
 65 70 75 80  
 Arg Tyr Gly Arg Arg Arg Pro Phe Ile Trp Ala Leu Ser Leu Gly Ile  
 85 90 95  
 Leu Leu Ser Leu Phe Leu Ile Pro Arg Ala Gly Trp Leu Ala Gly Leu  
 100 105 110  
 Leu Cys Pro Asp Pro Arg Pro Leu Glu Leu Ala Leu Leu Ile Leu Gly  
 115 120 125  
 Val Gly Leu Leu Asp Phe Cys Gly Gln Val Cys Phe Thr Pro Leu Glu  
 130 135 140  
 Ala Leu Leu Ser Asp Leu Phe Arg Asp Pro Asp His Cys Arg Gln Ala  
 145 150 155 160  
 Tyr Ser Val Tyr Ala Phe Met Ile Ser Leu Gly Gly Cys Leu Gly Tyr  
 165 170 175  
 Leu Leu Pro Ala Ile Asp Trp Asp Thr Ser Ala Leu Ala Pro Tyr Leu  
 180 185 190  
 Gly Thr Gln Glu Glu Cys Leu Phe Gly Leu Leu Thr Leu Ile Phe Leu  
 195 200 205  
 Thr Cys Val Ala Ala Thr Leu Leu Val Ala Glu Glu Ala Ala Leu Gly  
 210 215 220  
 Pro Thr Glu Pro Ala Glu Gly Leu Ser Ala Pro Ser Leu Ser Pro His  
 225 230 235 240  
 Cys Cys Pro Cys Arg Ala Arg Leu Ala Phe Arg Asn Leu Gly Ala Leu

43

				245					250					255	
Leu	Pro	Arg	Leu	His	Gln	Leu	Cys	Cys	Arg	Met	Pro	Arg	Thr	Leu	Arg
			260					265					270		
Arg	Leu	Phe	Val	Ala	Glu	Leu	Cys	Ser	Trp	Met	Ala	Leu	Met	Thr	Phe
		275					280					285			
Thr	Leu	Phe	Tyr	Thr	Asp	Phe	Val	Gly	Glu	Gly	Leu	Tyr	Gln	Gly	Val
	290				295						300				
Pro	Arg	Ala	Glu	Pro	Gly	Thr	Glu	Ala	Arg	Arg	His	Tyr	Asp	Glu	Gly
305					310					315				320	
Val	Arg	Met	Gly	Ser	Leu	Gly	Leu	Phe	Leu	Gln	Cys	Ala	Ile	Ser	Leu
				325					330					335	
Val	Phe	Ser	Leu	Val	Met	Asp	Arg	Leu	Val	Gln	Arg	Phe	Gly	Thr	Arg
			340					345					350		
Ala	Val	Tyr	Leu	Ala	Ser	Val	Ala	Ala	Phe	Pro	Val	Ala	Ala	Gly	Ala
		355					360					365			
Thr	Cys	Leu	Ser	His	Ser	Val	Ala	Val	Val	Thr	Ala	Ser	Ala	Ala	Leu
	370					375					380				
Thr	Gly	Phe	Thr	Phe	Ser	Ala	Leu	Gln	Ile	Leu	Pro	Tyr	Thr	Leu	Ala
385					390					395				400	
Ser	Leu	Tyr	His	Arg	Glu	Lys	Gln	Val	Phe	Leu	Pro	Lys	Tyr	Arg	Gly
			405						410					415	
Asp	Thr	Gly	Gly	Ala	Ser	Ser	Glu	Asp	Ser	Leu	Met	Thr	Ser	Phe	Leu
			420					425					430		
Pro	Gly	Pro	Lys	Pro	Gly	Ala	Pro	Phe	Pro	Asn	Gly	His	Val	Gly	Ala
	435						440					445			
Gly	Gly	Ser	Gly	Leu	Leu	Pro	Pro	Pro	Pro	Ala	Leu	Cys	Gly	Ala	Ser
	450					455					460				
Ala	Cys	Asp	Val	Ser	Val	Arg	Val	Val	Val	Gly	Glu	Pro	Thr	Glu	Ala
465					470					475				480	
Arg	Val	Val	Pro	Gly	Arg	Gly	Ile	Cys	Leu	Asp	Leu	Ala	Ile	Leu	Asp
			485						490					495	
Ser	Ala	Phe	Leu	Ser	Gln	Val	Ala	Pro	Ser	Leu	Phe	Met	Gly	Ser	
			500					505					510		
Ile	Val	Gln	Leu	Ser	Gln	Ser	Val	Thr	Ala	Tyr	Met	Val	Ser	Ala	Ala
		515					520					525			
Gly	Leu	Gly	Leu	Val	Ala	Ile	Tyr	Phe	Ala	Thr	Gln	Val	Val	Phe	Asp
	530					535					540				
Lys	Ser	Asp	Leu	Ala	Lys	Tyr	Ser	Ala							
545					550										

&lt;210&gt; 114

&lt;211&gt; 241

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 114

Met	Gln	Cys	Phe	Ser	Phe	Ile	Lys	Thr	Met	Met	Ile	Leu	Phe	Asn	Leu
1				5					10					15	
Leu	Ile	Phe	Leu	Cys	Gly	Ala	Ala	Leu	Leu	Ala	Val	Gly	Ile	Trp	Val
			20					25				30			
Ser	Ile	Asp	Gly	Ala	Ser	Phe	Leu	Lys	Ile	Phe	Gly	Pro	Leu	Ser	Ser
		35					40					45			
Ser	Ala	Met	Gln	Phe	Val	Asn	Val	Gly	Tyr	Phe	Leu	Ile	Ala	Ala	Gly
	50					55					60				
Val	Val	Val	Phe	Ala	Leu	Gly	Phe	Leu	Gly	Cys	Tyr	Gly	Ala	Lys	Thr
65					70					75				80	
Glu	Ser	Lys	Cys	Ala	Leu	Val	Thr	Phe	Phe	Phe	Ile	Leu	Leu	Leu	Ile
				85					90					95	

Phe Ile Ala Glu Val Ala Ala Ala Val Val Ala Leu Val Tyr Thr Thr  
                   100                                  105                  110  
 Met Ala Glu His Phe Leu Thr Leu Leu Val Val Pro Ala Ile Lys Lys  
                   115                                  120                  125  
 Asp Tyr Gly Ser Gln Glu Asp Phe Thr Gln Val Trp Asn Thr Thr Met  
                   130                                  135                  140  
 Lys Gly Leu Lys Cys Cys Gly Phe Thr Asn Tyr Thr Asp Phe Glu Asp  
                   145                                  150                  155                  160  
 Ser Pro Tyr Phe Lys Glu Asn Ser Ala Phe Pro Pro Phe Cys Cys Asn  
                                   165                                  170                  175  
 Asp Asn Val Thr Asn Thr Ala Asn Glu Thr Cys Thr Lys Gln Lys Ala  
                                   180                                  185                  190  
 His Asp Gln Lys Val Glu Gly Cys Phe Asn Gln Leu Leu Tyr Asp Ile  
                                   195                                  200                  205  
 Arg Thr Asn Ala Val Thr Val Gly Gly Val Ala Ala Gly Ile Gly Gly  
                                   210                                  215                  220  
 Leu Glu Leu Ala Ala Met Ile Val Ser Met Tyr Leu Tyr Cys Asn Leu  
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 Gln

<210> 115  
 <211> 366  
 <212> DNA  
 <213> Homo sapien

<400> 115  
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 ttggtttgtg aatccatctt gctttttccc cattggaact agtcattaac ccatctctga 180  
 actggtagaa aaacatctga agagctagtc tatcagcatc tgacagggtga attggatggt 240  
 tctcagaacc atttcaccca gacagcctgt ttctatcctg ttttaataaat tagtttgggt 300  
 tctctacatg cataacaaac cctgtctcaa tctgtcacat aaaagtctgt gacttgaagt 360  
 ttagtc 366

<210> 116  
 <211> 282  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(282)  
 <223> n = A,T,C or G  
 <400> 116  
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 gagaaatgag atnaaacaca atnttataaa gtctacttag agaagatcaa gtgacctcaa 120  
 agactttact attttcatat tttaagacac atgatttatc ctatttttagt aacctgggtc 180  
 atacgttaaa caaaggataa tgtgaacagc agagaggatt tgttggcaga aaatctatgt 240  
 tcaatctnga actatctana tcacagacat ttctattcct tt 282

<210> 117  
 <211> 305  
 <212> DNA  
 <213> Homo sapien

<220>

45

<221> misc\_feature  
 <222> (1)...(305)  
 <223> n = A,T,C or G

<400> 117  
 acacatgtcg cttcactgcc ttcttagatg cttctggtca acatanagga acagggacca 60  
 tatttatcct cctcctgaa acaattgcaa aataanacaa aatatatgaa acaattgcaa 120  
 aataaggcaa aatatatgaa acaacaggtc togagatatt ggaaatcagt caatgaagga 180  
 tactgatccc tgatcactgt cctaattgcag gatgtgggaa acagatgagg tcacctctgt 240  
 gactgccccca gcttactgcc tgtagagagt ttctangctg cagttcagac agggagaaat 300  
 tgggt 305

<210> 118  
 <211> 71  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(71)  
 <223> n = A,T,C or G

<400> 118  
 accaaggtgt ntgaatctct gacgtgggga tctctgattc ccgcacaatc tgagtggaaa 60  
 aantcctggg t 71

<210> 119  
 <211> 212  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(212)  
 <223> n = A,T,C or G

<400> 119  
 actccggttg gtgtcagcag cacgtggcat tgaacatngc aatgtggagc ccaaaccaca 60  
 gaaaatgggg tgaaattggc caactttcta tnaacttatg ttggcaantt tgccaccaac 120  
 agtaagctgg cccttctaataaaaagaaaat tgaaagggtt ctcactaanc ggaattaant 180  
 aatggantca aganactccc aggcctcagc gt 212

<210> 120  
 <211> 90  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(90)  
 <223> n = A,T,C or G

<400> 120  
 actcgttgca natcaggggc cccccagagt caccgttgca ggagtccttc tggctcttggc 60  
 ctccgccggc gcagaacatg ctggggtgggt 90

<210> 121  
 <211> 218

46

<212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(218)  
 <223> n = A,T,C or G

<400> 121  
 tgtancgtga anacgacaga nagggttgtc aaaaatggag aanccttgaa gtcattttga 60  
 gaataagatt tgctaaaaga tttggggcta aaacatgggtt attgggagac atttctgaag 120  
 atatncangt aaattangga atgaattcat ggttcttttg ggaattcctt tacgatngcc 180  
 agcatanact tcatgtgggg atancagcta cccttgta 218

<210> 122  
 <211> 171  
 <212> DNA  
 <213> Homo sapien

<400> 122  
 taggggtgta tgcaactgta aggacaaaaa ttgagactca actggcttaa ccaataaagg 60  
 catttgtag ctcatggaac aggaagtcgg atggtggggc atcttcagtg ctgcatgagt 120  
 caccaccccg gcggggtcat ctgtgccaca ggtccctgtt gacagtgcgg t 171

<210> 123  
 <211> 76  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(76)  
 <223> n = A,T,C or G

<400> 123  
 tgtagcgtga agacnacaga atggtgtgtg ctgtgctatc caggaacaca tttattatca 60  
 ttatcaanta ttgtgt 76

<210> 124  
 <211> 131  
 <212> DNA  
 <213> Homo sapien

<400> 124  
 acctttcccc aaggccaatg tcctgtgtgc taactggccg gctgcaggac agctgcaatt 60  
 caatgtgctg ggtcatatgg aggggaggag actctaaaat agccaatttt attctcttgg 120  
 ttaagatttg t 131

<210> 125  
 <211> 432  
 <212> DNA  
 <213> Homo sapien

<400> 125  
 actttatcta ctggctatga aatagatggt ggaaaattgc gttaccaact ataccactgg 60  
 cttgaaaaag aggtgatagc tcttcagagg acttgtgact ttgtctcaga tgctgaagaa 120  
 ctacagtctg catttggcag aaatgaagat gaatttggat taaatgagga tgctgaagat 180  
 ttgcctcacc aaacaaaagt gaaacaactg agagaaaatt ttcaggaaaa aagacagtgg 240

```

ctcttgaagt atcagtcact tttgagaatg tttcttagtt actgcatact tcatggatcc 300
catggtgggg gtcttgcacg tgtaagaatg gaattgattt tgcttttgca agaattctcag 360
caggaaacat cagaaccact attttctagc cctctgtcag agcaaaccctc agtgcctctc 420
ctctttgctt gt 432

```

```

<210> 126
<211> 112
<212> DNA
<213> Homo sapien

```

```

<400> 126
acacaacttg aatagtaaaa tagaaactga gctgaaattt ctaattcact ttctaaccat 60
agtaagaatg atatttcccc ccagggatca ccaaatattt ataaaaattt gt 112

```

```

<210> 127
<211> 54
<212> DNA
<213> Homo sapien

```

```

<400> 127
accacgaaac cacaacaag atggaagcat caatccactt gccaagcaca gcag 54

```

```

<210> 128
<211> 323
<212> DNA
<213> Homo sapien

```

```

<400> 128
acctcattag taattgtttt gttgtttcat ttttttctaa tgtctcccct ctaccagctc 60
acctgagata acagaatgaa aatggaagga cagccagatt tctcctttgc tctctgctca 120
ttctctctga agtctaggtt acccattttg gggaccattt ataggcaata aacacagttc 180
ccaaagcatt tggacagttt cttgtttgtg tttagaatgg ttttcctttt tcttagcctt 240
ttcctgcaaa aggtctcactc agtcccttgc ttgctcagtg gactgggctc cccagggcct 300
aggtctgcctt cttttccatg tcc 323

```

```

<210> 129
<211> 192
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(192)
<223> n = A,T,C or G

```

```

<400> 129
acatacatgt gtgtatatatt ttaaatatca cttttgtatc actctgactt tttagcatatc 60
tgaaaacaca ctaacataat ttntgtgaac catgatcaga tacaacccaa atcattcatc 120
tagcacattc atctgtgata naaagatagg tgagtttcat ttccttcacg ttggccaatg 180
gataaacaaa gt 192

```

```

<210> 130
<211> 362
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature

```



48

&lt;222&gt; (1)...(362)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 130

ccctttttta	tggaatgagt	agactgtatg	tttgaanatt	tanccacaac	ctctttgaca	60
tataatgacg	caacaaaaag	gtgctgttta	gtcctatggg	tcagtttatg	cccctgacaa	120
gtttocattg	tgttttgccc	atctttctgg	taatcgtggg	atcctccatg	ttattagtaa	180
ttctgtattc	cattttgtta	acgcctggta	gatgtaacct	gctangaggc	taactttata	240
cttattttaa	agctcttatt	ttgtgggtcat	taaaatggca	atttatgtgc	agcactttat	300
tgcagcagga	agcacgtgtg	ggttggttgt	aaagctcttt	gctaattcta	aaaagtaatg	360
gg						362

&lt;210&gt; 131

&lt;211&gt; 332

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(332)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 131

ctttttgaaa	gatcgtgtcc	actcctgtgg	acatcttgtt	ttaatggagt	ttcccatgca	60
gtangactgg	tatggttgca	gctgtccaga	taaaaacatt	tgaagagctc	caaaatgaga	120
gttctcccag	gttcgcctcg	ctgctccaag	tctcagcagc	agcctctttt	aggaggcatc	180
ttctgaacta	gattaaggca	gcttgtaa	ctgatgtgat	ttggtttatt	atccaactaa	240
cttccatctg	ttatcactgg	agaaagccca	gactcccan	gacnggtacg	gattgtgggc	300
atanaaggat	tgggtgaagc	tggcgttgtg	gt			332

&lt;210&gt; 132

&lt;211&gt; 322

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(322)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 132

acttttgcca	ttttgtatat	ataaacaatc	ttgggacatt	ctcctgaaaa	ctaggtgtcc	60
agtggctaag	agaactcgat	ttcaagcaat	tctgaaagga	aaaccagcat	gacacagaat	120
ctcaaattcc	caaacagggg	ctctgtggga	aaaatgaggg	aggacctttg	tatctcgggt	180
tttagcaagt	taaaatgaan	atgacaggaa	aggcttattt	atcaacaaag	agaagagttg	240
ggatgcttct	aaaaaaaaact	ttggtagaga	aaataggaat	gctnaatcct	agggaagcct	300
gtaacaatct	acaattggtc	ca				322

&lt;210&gt; 133

&lt;211&gt; 278

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(278)

&lt;223&gt; n = A,T,C or G

<400> 133  
 acaagccttc acaagtttaa ctaaattggg attaatcttt ctgtanttat ctgcataatt 60  
 cttgtttttc tttccatctg gctcctgggt tgacaatttg tggaaacaac tctattgcta 120  
 ctatttataa aaaatcacia atctttccct ttaagctatg ttnaattcaa actattcctg 180  
 ctattcctgt tttgtcaaag aaattatatt tttcaaaata tgtntatttg tttgatgggt 240  
 cccacgaaac actaataaaa accacagaga ccagcctg 278

<210> 134  
 <211> 121  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(121)  
 <223> n = A,T,C or G

<400> 134  
 gtttanaaaa cttgttttagc tccatagagg aaagaatggt aaactttgta ttttaaaaca 60  
 tgattctctg aggttaaact tggttttcaa atgttatttt tacttgtatt ttgcttttgg 120  
 t 121

<210> 135  
 <211> 350  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(350)  
 <223> n = A,T,C or G

<400> 135  
 acttanaacc atgcctagca catcagaatc cctcaaagaa catcagtata atcctataacc 60  
 atancaagtg gtgactgggt aagcgtgcga caaaggctcag ctggcacatt acttgtgtgc 120  
 aaacttgata cttttgttct aagtaggaac tagtatacag tncctaggan tggtagtcca 180  
 ggggtgcccc caactcctgc agccgctcct ctgtgccagn ccctgnaagg aactttcgtc 240  
 ccacctcaat caagccctgg gccatgctac ctgcaatttg ctgaacaaac gtttgctgag 300  
 ttcccaagga tgcaaagcct ggtgctcaac tcttggggag tcaactcagt 350

<210> 136  
 <211> 399  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(399)  
 <223> n = A,T,C or G

<400> 136  
 tgtaccgtga agacgacaga agttgcatgg cagggacagg gcagggccga ggccaggggt 60  
 gctgtgattg tatccgaata ntccctcgtga gaaaagataa tgagatgacg tgagcagcct 120  
 gcagacttgt gtctgccttc aanaagccag acaggaaggc cctgcctgcc ttggctctga 180  
 cctggcggcc agccagccag ccacaggtgg gcttcttcct tttgtggtga caacnccaag 240  
 aaaactgcag aggccaggg tcaggtgtna gtgggtangt gaccataaaa caccaggtgc 300  
 tcccaggaac ccgggcaaag gccatcccca cctacagcca gcatgcccac tggcgtgatg 360  
 ggtgcagang gatgaagcag ccagntgttc tgctgtggt 399

50

<210> 137  
 <211> 165  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(165)  
 <223> n = A,T,C or G

<400> 137  
 actggtgtgg tngggggtga tgctggtggt anaagttgan gtgacttcan gatggtgtgt 60  
 ggaggaagtg tgtgaacgta gggatgtaga ngttttggcc gtgctaaatg agcttcggga 120  
 ttggctggtc ccactggtgg tcaactgtcat tgggtggggt cctgt 165

<210> 138  
 <211> 338  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(338)  
 <223> n = A,T,C or G

<400> 138  
 actcactgga atgccacatt cacaacagaa tcagaggtct gtgaaaacat taatggctcc 60  
 ttaacttctc cagtaagaat cagggacttg aaatggaaac gttaacagcc acatgcccac 120  
 tgctgggcag tctcccatgc cttccacagt gaaagggctt gagaaaaatc acatccaatg 180  
 tcatgtgttt ccagccacac caaaaggtgc ttggggtgga gggctggggg catananggt 240  
 cangcctcag gaagcctcaa gttccattca gctttgccac tgtacattcc ccatntttaa 300  
 aaaaactgat gccttttttt tttttttttg taaaattc 338

<210> 139  
 <211> 382  
 <212> DNA  
 <213> Homo sapien

<400> 139  
 gggaatcttg gtttttggca tctggtttgc ctatagccga ggccactttg acagaacaaa 60  
 gaaagggact tcgagtaaga aggtgattta cagccagcct agtgcccgaa gtgaaggaga 120  
 attcaaacag acctcgatcat tcttggtgtg agcctggctg gctcaccgcc tatcatctgc 180  
 atttgcttca ctcagggtgct accggactct ggccctgat gtctgtagtt tcacaggatg 240  
 ccttattttgt cttctacacc ccacagggcc cctacttct tcggatgtgt ttttaataat 300  
 gtcagctatg tgccccatcc tccttcacgc cctccctccc tttcctacca ctgctgagtg 360  
 gcctggaact tgtttaaagt gt 382

<210> 140  
 <211> 200  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(200)  
 <223> n = A,T,C or G

<400> 140  
 accaaanctt ctttctgttg tgttngattt tactataggg gtttngcttn ttctaaanat 60  
 acttttcatt taacancatt tgtaaagtgt caggctgcac ttgctccat anaattattg 120  
 ttttcacatt tcaacttgta tgtgtttgtc tcttanagca ttggtgaaat cacatatttt 180  
 atattcagca taaaggagaa 200

<210> 141  
 <211> 335  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(335)  
 <223> n = A,T,C or G

<400> 141  
 acttttattt caaaacactc atatgttgca aaaaacacat agaaaaataa agtttggttg 60  
 ggggtgctgac taaacttcaa gtcacagact tttatgtgac agattggagc aggggtttgtt 120  
 atgcatgtag agaaccctaa ctaatttatt aaacaggata gaaacaggct gtctgggtga 180  
 aatgggtctg agaaccatcc aattcacctg tcagatgctg atanactagc tcttcagatg 240  
 tttttctacc agttcagaga tnggttaatg actanttcca atgggggaaa agcaagatgg 300  
 attcacaac caagtaattt taaacaaaga cactt 335

<210> 142  
 <211> 459  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(459)  
 <223> n = A,T,C or G

<400> 142  
 accagggttaa tattgccaca tatatccttt ccaattgcgg gctaaacaga cgtgtattta 60  
 ggggtgtttaa aagacaacc agcttaatat caagagaaat tgtgacctt catggagtat 120  
 ctgatggaga aaacactgag ttttgacaaa tottatttta ttcagatagc agtctgatca 180  
 cacatggtcc aacaacactc aaataataaa tcaaataatna tcagatgtta aagattggtc 240  
 ttcaaacatc atagccaatg atgcccgcgt tgcctataat ctctccgaca taaaaccaca 300  
 tcaacacctc agtggccacc aaaccattca gcacagcttc cttaactgtg agctgtttga 360  
 agctaccagt ctgagcacta ttgactatnt ttttcangct ctgaatagct ctagggatct 420  
 cagcanggtt gggaggaacc agctcaacct tggcgtant 459

<210> 143  
 <211> 140  
 <212> DNA  
 <213> Homo sapien

<400> 143  
 acatttcctt ccaccaagtc aggactcctg gcttctgtgg gagttcttat cacctgaggg 60  
 aaatccaaac agtctctcct agaaaggaat agtgtcacca accccacca totccctgag 120  
 accatccgac ttccctgtgt 140

<210> 144  
 <211> 164  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(164)  
 <223> n = A,T,C or G

<400> 144  
 acttcagtaa caacatacaa taacaacatt aagtgtatat tgccatcttt gtcattttct 60  
 atctatacca ctctcccttc tgaaaacaan aatcactanc caatcactta tacaaatttg 120  
 aggcaattaa tccatatttg ttttcaataa ggaaaaaaag atgt 164

<210> 145  
 <211> 303  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(303)  
 <223> n = A,T,C or G

<400> 145  
 acgtagacca tccaactttg tatttgtaat ggcaaacatc cagnagcaat tcctaaacaa 60  
 actggagggt atttataccc aattatccca ttcattaaca tgccctcctc ctcaggctat 120  
 gcaggacagc tatcataagt cggcccaggc atccagatac taccatttgt ataaacttca 180  
 gtaggggagt ccatccaagt gacaggtcta atcaaaggag gaaatggaac ataagcccag 240  
 tagtaaaatn ttgcttagct gaaacagcca caaaagactt accgcctgtg tgattaccat 300  
 caa 303

<210> 146  
 <211> 327  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(327)  
 <223> n = A,T,C or G

<400> 146  
 actgcagctc aattagaagt ggtctctgac tttcatcanc ttctccctgg gctccatgac 60  
 actggcctgg agtgactcat tgctctgggt ggttgagaga gtccttttgc caacaggcct 120  
 ccaagtcagg gctgggattt gtttcccttc cacattctag caacaatatg ctggccactt 180  
 cctgaacagg gaggggtgga ggagccagca tggaacaagc tgccactttc taaagtagcc 240  
 agacttgccc ctgggcctgt cacacctact gatgaccttc tgtgcctgca ggatggaatg 300  
 taggggtgag ctgtgtgact ctatggt 327

<210> 147  
 <211> 173  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(173)  
 <223> n = A,T,C or G

<400> 147

```

acattgtttt tttgagataa agcattgana gagctctcct taacgtgaca caatggaagg      60
actggaacac atacccacat ctttgttctg agggataatt ttctgataaa gtcttgctgt      120
atattcaagc acatatgtta tatattattc agttccatgt ttatagccta gtt              173

```

<210> 148

<211> 477

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(477)

<223> n = A,T,C or G

<400> 148

```

acaaccactt tatctcatcg aatttttaac ccaaactcac tcaactgtgcc tttctatcct      60
atgggatata ttatttgatg ctccatttca tcacacatat atgaataata cactcatact      120
gccctactac ctgctgcaat aatcacattc ccttcctgtc ctgaccctga agccattggg      180
gtggctcctag tggccatcag tccangcctg caccttgagc ccttgagctc cattgctcac      240
nccanccac ctcaccgacc ccacccctct acacagctac ctcccttgctc tctaacccca      300
tagattatnt ccaaattcag tcaattaagt tactattaac actctacccg acatgtccag      360
caccactggt aagccttctc cagccaacac acacacacac acacncacac acacacatat      420
ccaggcacag gctacctcat cttcacaatc acccctttaa ttaccatgct atggtgg        477

```

<210> 149

<211> 207

<212> DNA

<213> Homo sapien

<400> 149

```

acagttgtat tataatatca agaaataaac ttgcaatgag agcattttaag agggaagaac      60
taacgtatatt tagagagcca aggaaggttt ctgtggggag tgggatgtaa ggtggggcct      120
gatgataaat aagagtcagc caggtaagtg ggtggtgtgg tatgggcaca gtgaagaaca      180
tttcaggcag agggaacagc agtgaaa

```

<210> 150

<211> 111

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(111)

<223> n = A,T,C or G

<400> 150

```

accttgatatt cattgctgct ctgatggaaa cccaactatc taatttagct aaaacatggg      60
cacttaaatg tggtcagtgt ttggacttgt taactantgg catctttggg t              111

```

<210> 151

<211> 196

<212> DNA

<213> Homo sapien

<400> 151

```

agcgcggcag gtcatttga acattccaga tacctatcat tactcgatgc tgttgataac      60
agcaagatgg ctttgaactc agggtcacca ccagctattg gaccttacta tgaaaaccat      120
ggataccaac cggaaaaccc ctatcccgcg cagcccactg tgggtccccc tgtctacgag      180

```

gtgcatccgg ctcagt 196

<210> 152  
 <211> 132  
 <212> DNA  
 <213> Homo sapien

<400> 152  
 acagcacttt cacatgtaag aagggagaaa ttcctaaatg taggagaaag ataacagAAC 60  
 ctcccccttt tcatctagtG gtggaaacct gatgctttat gttgacagga atagaaccag 120  
 gagggagttt gt 132

<210> 153  
 <211> 285  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(285)  
 <223> n = A,T,C or G

<400> 153  
 acaanacceca nganaggcca ctggccgtgg tgtcatggcc tccaaacatg aaagtgtcag 60  
 cttctgctct tatgtcctca tctgacaact ctttaccatt tttatocctg ctcagcagga 120  
 gcacatcaat aaagtccaaa gtcttggact tggccttggc ttggaggaag tcatcaacac 180  
 cctggctagt gagggtgcgg cgccgtcctt ggatgacggc atctgtgaag tcgtgcacca 240  
 gtctgcaggc cctgtggaag cgccgtccac acggagtnag gaatt 285

<210> 154  
 <211> 333  
 <212> DNA  
 <213> Homo sapien

<400> 154  
 accacagtcc tggtgggcca gggcttcatg accctttctg tgaaaagcca tattatcacc 60  
 accccaaatt tttccttaaa tatctttaac tgaaggggtc agcctottga ctgcaaagac 120  
 cctaagccgg ttacacagct aactccact ggccctgatt tgtgaaattg ctgctgcctg 180  
 attggcacag gagtgcgaagg tgttcagctc ccctcctcgg tggaaagaga ctctgatttg 240  
 agtttcacaa attctcgggc cacctcgtca ttgtcctctt gaaataaaat ccggagaatg 300  
 gtcaggcctg tctcatccat atggatcttc cgg 333

<210> 155  
 <211> 308  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(308)  
 <223> n = A,T,C or G

<400> 155  
 actggaaata ataaaacceca catcacagtG ttgtgtcaaa gatcatcagg gcatggatgg 60  
 gaaagtgctt tgggaactgt aaagtgccta acacatgatc gatgattttt gttataatat 120  
 ttgaatcacg gtgcatacaa actctcctgc ctgctcctcc tgggccccag cccagcccc 180  
 atcacagctc actgctctgt tcatccaggc ccagcatgta gtggctgatt cttcttggct 240  
 gcttttagcc tccanaagtt tctctgaagc caaccaaacc tctangtgta aggcagtctg 300

gccctggt 308

<210> 156  
 <211> 295  
 <212> DNA  
 <213> Homo sapien

<400> 156  
 accttgctcg gtgcttgga catattagga actcaaaata tgagatgata acagtgccta 60  
 ttattgatta ctgagagaac tgtagacat ttagttgaag attttctaca caggaaactga 120  
 gaataggaga ttatgtttgg ccctcatatt ctctcctatc ctccttgccct cattctatgt 180  
 ctaatatatt ctcaatcaaa taaggtttagc ataatcagga aatcgaccaa ataccaatat 240  
 aaaaccagat gtctatcctt aagattttca aatagaaaac aaattaacag actat 295

<210> 157  
 <211> 126  
 <212> DNA  
 <213> Homo sapien

<400> 157  
 acaagtttaa atagtgtgt cactgtgcat gtgtgaaat gtgaaatcca ccacatttct 60  
 gaagagcaaa acaaattctg tcatgtaatc tctatcttgg gtcgtgggta tatctgtccc 120  
 cttagt 126

<210> 158  
 <211> 442  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(442)  
 <223> n = A,T,C or G

<400> 158  
 acccactggt cttggaaca cccatcctta atacgatgat ttttctgtcg tgtgaaaatg 60  
 aanccagcag gctgcccta gtcagtcctt ccttcagag aaaaagagat ttgagaaagt 120  
 gcctgggtaa ttcaccatta atttcctccc ccaaactctc tgagtcttcc cttaatattt 180  
 ctggtggttc tgaccaaagc aggtcatggt ttgttgagca tttgggatcc cagtgaagta 240  
 natgtttgta gccttgcata cttagccctt cccacgcaca aacggagtgg cagagtgggtg 300  
 ccaaccctgt tttccagtc caggtagaca gattcacagt gcggaattct ggaagctgga 360  
 nacagacggg ctctttgcag agccgggact ctgagangga catgagggcc tctgcctctg 420  
 tgttcattct ctgatgtcct gt 442

<210> 159  
 <211> 498  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(498)  
 <223> n = A,T,C or G

<400> 159  
 acttcagggt aacgttggtt tttccgttga gcctgaactg atgggtgacg ttgtagggtc 60  
 tccaacaaga actgagggtt cagagcgggt aggggaagagt gctgttccag ttgcacctgg 120  
 gctgctgtgg actgttggtt attcctcact acggcccaag gttgtggaac tggcanaaag 180



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gtgtgttgtt gganttgagc tcgggcggtt gtggtaggtt gtgggctctt caacaggggc      240
tgctgtggtg ccgggangtg aangtggtgt gtcacttgag ctgggccagc tctggaaagt      300
antanattct tcctgaaggc cagcgcttgt ggagctggca ngggtcantg ttgtgtgtaa      360
cgaaccagtg ctgctgtggg tgggtgtana tcctccacaa agcctgaagt tatggtgtcn      420
tcaggtaana atgtggtttc agtgtccctg ggcngctgtg gaaggttgta nattgtcacc      480
aagggaataa gctgtggt

```

```

<210> 160
<211> 380
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(380)
<223> n = A,T,C or G

```

```

<400> 160
acctgcatcc agcttccctg ccaaactcac aaggagacat caacctctag acagggaaac      60
agcttcagga tacttcagg agacagagcc accagcagca aaacaaatat tcccatgcct      120
ggagcatggc atagaggaag ctganaaatg tggggtctga ggaagccatt tgagtctggc      180
cactagacat ctcatcagcc acttgtgtga agagatgcc catgacccca gatgcctctc      240
ccacccttac ctccatctca cacacttgag ctttccactc tgtataattc taacatcctg      300
gagaaaaatg gcagtttgac cgaacctgtt cacaacggta gaggctgatt tctaacgaaa      360
ctttagaat gaagcctgga

```

```

<210> 161
<211> 114
<212> DNA
<213> Homo sapien

```

```

<400> 161
actccacatc ccctctgagc aggcggttgt cgttcaaggt gtatttggcc ttgcctgtca      60
cactgtccac tggcccccta tccacttggt gcttaatccc tcgaaagagc atgt      114

```

```

<210> 162
<211> 177
<212> DNA
<213> Homo sapien

```

```

<400> 162
actttctgaa tcgaatcaaa tgatacttag tgtagtthta atatcctcat atatatcaaa      60
gttttactac tctgataatt ttgtaaacca ggtaaccaga acatccagtc atacagcttt      120
tggtgatata taacttggca ataaccagct ctggtgatac ataaaactac tcaactgt      177

```

```

<210> 163
<211> 137
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(137)
<223> n = A,T,C or G

```

```

<400> 163
catttataca gacaggcgtg aagacattca cgacaaaaac gcgaaattct atcccgtgac      60
canagaaggc agctaaggct actcctacat cctggcgtgg gtggccttgc cctgcacctt      120

```

catcagcggc atgatgt 137

<210> 164  
 <211> 469  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (469)  
 <223> n = A,T,C or G

<400> 164  
 ottatcacaa tgaatgttct cctgggcagc gttgtgatct ttgccacctt cgtgacttta 60  
 tgcaatgcat catgctatct cttacctaata gagggagttc caggagattc aaccaggaaa 120  
 tgcatggatc tcaaaggaaa caaacaccca ataaactcgg agtggcagac tgacaactgt 180  
 gagacatgca cttgctacga aacagaaatt tcatgttgca cccttgtttc tacacctgtg 240  
 ggttatgaca aagacaactg ccaaagaatc ttcaagaagg aggactgcaa gtatatcgtg 300  
 gtggagaaga aggacccaaa aaagacctgt tctgtcagtg aatggataat ctaatgtgct 360  
 tctagttagc acagggctcc caggccaggc ctcattctcc tctggcctct aatagtcaat 420  
 gattgtgtag ccattgcctat cagtaaaaag atntttgagc aaacacttt 469

<210> 165  
 <211> 195  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (195)  
 <223> n = A,T,C or G

<400> 165  
 acagtttttt atanatcgc acattgccgg cacttgtgtt cagtttcata aagctgggtg 60  
 atccgctgtc atccactatt ccttggctag agtaaaaatt attcttatag cccatgtccc 120  
 tgcaggccgc ccgcccgtag ttctcgttcc agtcgtcttg gcacacaggg tgccaggact 180  
 tcctctgaga tgagt 195

<210> 166  
 <211> 383  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (383)  
 <223> n = A,T,C or G

<400> 166  
 acatcttagt agtgtggcac atcagggggc catcagggtc acagtcactc atagcctcgc 60  
 cgaggctcga gtccacacca ccggtgtagg tgtgctcaat cttgggcttg gcgcccacct 120  
 ttggagaagg gatatgctgc acacacatgt ccacaaagcc tgtgaactcg ccaaagaatt 180  
 tttgcagacc agcctgagca aggggcggat gttcagcttc agtcctcctc tcgtcagggtg 240  
 gatgccaaac tcgtctangg tccgtgggaa gctgggtgtc acntcaccta caacctgggc 300  
 gangatctta taaagaggct ccnagataaa ctccacgaaa cttctctggg agctgctagt 360  
 nggggccttt ttggtgaact ttc 383

<210> 167

58

<211> 247  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(247)  
 <223> n = A,T,C or G

<400> 167  
 acagagccag accttggcca taaatgaanc agagattaag actaaacccc aagtcganat 60  
 tggagcagaa actggagcaa gaagtgggcc tggggctgaa gtagagacca aggccactgc 120  
 tatanccata cacagagcca actctcaggg caaggcnatg gttggggcag anccagagac 180  
 tcaatctgan tccaaagtgg tggctggaac actggctcatg acanaggcag tgactctgac 240  
 tgangtc 247

<210> 168  
 <211> 273  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(273)  
 <223> n = A,T,C or G

<400> 168  
 acttctaagt tttctagaag tggaaggatt gtantcatcc tgaaaatggg tttacttcaa 60  
 aatccctcan ccttgttctt cactactgtc tatactgana gtgtcatgtt tccacaaagg 120  
 gctgacacct gagcctgnat tttcactcat ccctgagaag ccctttccag taggggtggc 180  
 aattcccaac ttccttgcca caagcttccc aggctttctc ccctgggaaa ctccagcttg 240  
 agtcccagat acactcatgg gctgccctgg gca 273

<210> 169  
 <211> 431  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(431)  
 <223> n = A,T,C or G

<400> 169  
 acagccttgg cttccccaac ctccacagtc tcagtgcaga aagatcatct tccagcagtc 60  
 agctcagacc aggggtcaaag gatgtgacat caacagtttc tgggtttcaga acagggttcta 120  
 ctactgtcaa atgacccccc atacttcctc aaaggctgtg gtaagttttg cacagggtgag 180  
 ggcagcagaa aggggggtant tactgatgga caccatcttc tctgtatact ccaactgac 240  
 cttgccatgg gcaaaaggcc ctaccacaaa aacaatagga tcaactgctgg gcaccagctc 300  
 acgcacatca ctgacaaccg ggatggaaaa agaantgcc aactttcatac atccaactgg 360  
 aaagtgatct gatactggat tottaattac cttcaaaagc ttctgggggc catcagctgc 420  
 tcgaacactg a 431

<210> 170  
 <211> 266  
 <212> DNA  
 <213> Homo sapien

59

<220>  
 <221> misc\_feature  
 <222> (1)...(266)  
 <223> n = A,T,C or G

<400> 170  
 acctgtgggc tgggctgtta tgccgtgtgcc ggctgctgaa agggagttca gaggtggagc 60  
 tcaaggagct ctgcaggcat tttgccaaanc ctctccanag canagggagc aacctacact 120  
 ccccgctaga aagacaccag attggagtcc tgggaggggg agttgggggtg ggcatttgat 180  
 gtatacttgt cacctgaatg aangagccag agaggaanga gacgaanatg anattggcct 240  
 tcaaagctag gggctctggca ggtgga 266

<210> 171  
 <211> 1248  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(1248)  
 <223> n = A,T,C or G

<400> 171  
 ggcagccaaa tcataaacgg cgaggactgc agcccgcact cgcagccctg gcaggcggca 60  
 ctggctcatgg aaaacgaatt gttctgctcg ggcgctcctgg tgcattccgca gtgggtgctg 120  
 tcagccgcac actgtttcca gaagtgtgtg cagagctcct acaccatcgg gctgggcctg 180  
 cacagtcttg aggccgacca agagccaggg agccagatgg tggaggccag cctctccgta 240  
 cggcaccag agtagaacag acccttgctc gctaacgacc tcatgctcat caagttggac 300  
 gaatccgtgt ccgagtctga caccatccgg agcatcagca ttgcttcgca gtgccctacc 360  
 gcggggaaact cttgcctcgt ttctggctgg ggtctgctgg cgaacggcag aatgcctacc 420  
 gtgctgcagt gcgtgaacgt gtcggtgggtg tctgaggagg tctgcagtaa gctctatgac 480  
 ccgctgtacc accccagcat gttctgcgcc ggcgaggggc aagaccagaa ggactcctgc 540  
 aacggtgact ctggggggcc cctgatctgc aacgggtact tgcagggcct tgtgtctttc 600  
 ggaaaagccc cgtgtggcca agttggcgtg ccagggtgtct acaccaacct ctgcaaattc 660  
 actgagtgya tagagaaaac cgtccaggcc agttaactct ggggactggg aacctatgaa 720  
 attgaccccc aaatacatcc tgcggaagga attcaggaat atctgttccc agcccctcct 780  
 ccctcaggcc caggagtcca ggccccagc ccctcctccc tcaaaccaag ggtacagatc 840  
 ccagcccct cctccctcag acccaggagt ccagaccccc cagcccctcc tccctcagac 900  
 ccaggagtcc agcccctcct ccctcagacc caggagtcca gacccccag cccctcctcc 960  
 ctacagacca ggggtccagg cccccaaccc ctccctccctc agactcagag gtccaagcco 1020  
 ccaaccntc attccccaga cccagaggtc cagggtcccag cccctcntcc ctacagacca 1080  
 gcggtccaat gccacctaga ctntccctgt acacagtgcc cccttggtggc acgttgacct 1140  
 aaccttacca gttggttttt catttttngt ccctttcccc tagatccaga aataaagttt 1200  
 aagagaagng caaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaa 1248

<210> 172  
 <211> 159  
 <212> PRT  
 <213> Homo sapien

<220>  
 <221> VARIANT  
 <222> (1)...(159)  
 <223> Xaa = Any Amino Acid

<400> 172  
 Met Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro  
 1 5 10 15

60

Leu Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser  
                   20                  25                  30  
 Glu Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr  
                   35                  40                  45  
 Ala Gly Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly  
                   50                  55                  60  
 Arg Met Pro Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu  
                   65                  70                  75                  80  
 Glu Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe  
                   85                  90                  95  
 Cys Ala Gly Gly Gly Gln Xaa Gln Xaa Asp Ser Cys Asn Gly Asp Ser  
                   100                  105                  110  
 Gly Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe  
                   115                  120                  125  
 Gly Lys Ala Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn  
                   130                  135                  140  
 Leu Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser  
                   145                  150                  155

<210> 173  
 <211> 1265  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(1265)  
 <223> n = A,T,C or G

<400> 173  
 ggcagccgc actcgcagcc ctggcaggcg gcaactgggtca tggaaaacga attgttctgc 60  
 tcgggagctcc tgggtgcatcc gcagtgagggtg ctgtcagccg cacactgttt ccagaactcc 120  
 tacaccatcg ggctgggcct gcacagtctt gaggccgacc aagagccagg gagccagatg 180  
 gtggaggcca gcctctccgt acggcaccga gactacaaca gacccttgct cgctaacgac 240  
 ctcatgctca tcaagttgga cgaatccgtg tccgagtctg acaccatccg gagcatcagc 300  
 attgcttcgc agtgccttac cgcggggaac tcttgccctg tttctggctg gggctctgctg 360  
 gcgaacggtg agctcacggg tgtgtgtctg ccctcttcaa ggaggtcctc tgcccagtcg 420  
 cgggggctga cccagagctc tgcgtcccag gcagaatgcc taccgtgctg cagtgcgtga 480  
 acgtgtcggg ggtgtctgag gaggtctgca gtaagctcta tgaccgctg taccacccca 540  
 gcatgttctg cgccggcgga gggcaagacc agaaggactc ctgcaacggg gactctgggg 600  
 ggcccctgat ctgcaacggg tacttgacgg gccttggtgtc tttcggaata gcccgtgtg 660  
 gccaaagtgg cgtgccagggt gtctacacca acctctgcaa attcactgag tggatagaga 720  
 aaaccgtcca ggccagttaa ctctggggac tgggaaccca tgaaattgac ccccaaatac 780  
 atcctgcgga aggaattcag gaatatctgt tcccagcccc tctcctccta ggcccaggag 840  
 tccaggcccc cagcccctcc tccctcaaac caagggtaca gatccccagc ccctcctccc 900  
 tcagaccagc gagtcacagc cccccagccc ctctcctc agaccagga gtccagcccc 960  
 tcctcctc gacccaggag tccagacccc ccagcccctc ctccctcaga cccagggggt 1020  
 gagggcccca accctcctc ctccagagtc agaggtccaa gcccacaacc cctcgttccc 1080  
 cagaccacaga ggttnnaggtc ccagcccctc ttccntcaga cccagnnggt caatgccacc 1140  
 tagattttcc ctgnacacag tgcccccttg tggngangtt acccaacctt accagttggg 1200  
 ttttcatttt tngtcccttt cccctagatc cagaaataaa gttaaagaga nngcaaaaa 1260  
 aaaaa 1265

<210> 174  
 <211> 1459  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(1459)  
 <223> n = A,T,C or G

<400> 174

ggtcagccgc	acactgtttc	cagaagtgag	tgcagagctc	ctacaccatc	gggctgggcc	60
tgcacagtct	tgaggccgac	caagagccag	ggagccagat	ggtggaggcc	agcctctccg	120
tacggcacc	agagtacaac	agacccttgc	tcgctaacga	cctcatgctc	atcaagttgg	180
acgaatccgt	gtccgagtct	gacaccatcc	ggagcatcag	cattgcttcg	cagtgcctta	240
ccgcggggaa	ctcttgctc	gtttctggct	gggtctgct	ggcgaacggt	gagctcacgg	300
gtgtgtgtct	gccctcttca	aggaggctct	ctgcccagtc	gcgggggctg	acccagagct	360
ctgcgtccca	ggcagaatgc	ctaccgtgct	gcagtgcgtg	aacgtgtcgg	tgggtgtctga	420
ngagggtctgc	antaagctct	atgacccgct	gtaccacccc	ancatgttct	gcgccggcgg	480
agggcaagac	cagaaggact	cctgcaacgt	gagagagggg	aaaggggagg	gcaggcgact	540
cagggaaagg	tggagaagg	ggagacagag	acacacaggg	ccgcatggcg	agatgcagag	600
atggagagac	acacagggag	acagtgacaa	ctagagagag	aaactgagag	aaacagagaa	660
ataaacacag	gaataaagag	aagcaaagga	agagagaaac	agaaacagac	atggggaggc	720
agaaacacac	acacatagaa	atgcagttga	ccttccaaca	gcatggggcc	tgagggcggg	780
gacctccacc	caatagaaaa	tcctcttata	acttttgact	ccccaaaaac	ctgactagaa	840
atagcctact	gttgacgggg	agccttacca	ataacataaa	tagtcgattt	atgcatacgt	900
tttatgcatt	catgatatac	ctttgttga	attttttgat	atttctaagc	tacacagttc	960
gtctgtgaat	ttttttaaat	tgttgcaact	ctcctaaaat	ttttctgatg	tgttttattga	1020
aaaaatccaa	gtataagtgg	acttgtgcat	tcaaacagg	gttgttcaag	ggtcaactgt	1080
gtacccagag	ggaaacagtg	acacagattc	atagagggtga	aacacgaaga	gaaacaggaa	1140
aaatcaagac	tctacaaaga	ggctgggcag	ggtggctcat	gcctgtaatc	ccagcacttt	1200
gggaggcgag	gcaggcagat	cacttgaggt	aaggagttca	agaccagcct	ggccaaaatg	1260
gtgaaatcct	gtctgtacta	aaaatacaaa	agttagctgg	atatgggtgc	aggcgccctgt	1320
aatcccagct	acttgggagg	ctgaggcagg	agaattgctt	gaatatggga	ggcagagggtt	1380
gaagtgagtt	gagatcacac	cactatactc	cagctggggc	aacagagtaa	gactctgtct	1440
caaaaaaaaa	aaaaaaaaa					1459

<210> 175  
 <211> 1167  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(1167)  
 <223> n = A,T,C or G

<400> 175

gcgcagccct	ggcaggcggc	actggctcatg	gaaaacgaat	tgttctgctc	gggcgtcctg	60
gtgcatccgc	agtgggtgct	gtcagccgca	cactgtttcc	agaactccta	caccatcggg	120
ctgggcctgc	acagtcttga	ggccgaccaa	gagccaggga	gccagatggt	ggaggccagc	180
ctctccgtac	ggcaccacaga	gtacaacaga	ctcttgctcg	ctaacgacct	catgctcatc	240
aagttggacg	aatccgtgtc	cgagtctgac	accatccgga	gcatacagcat	tgcttcgcag	300
tgccctaccg	cggggaaactc	ttgcctcgtn	cttggtctgg	gtctgctggc	gaacggcaga	360
atgcctaccg	tgctgactg	cgtgaacgtg	tcgggtggtg	ctgaggangt	ctgcagtaag	420
ctctatgacc	cgctgtacca	ccccagcatg	ttctgcgcgc	gcggaggggca	agaccagaag	480
gactcctgca	acgggtgactc	tggggggccc	ctgatctgca	acgggtactt	gcagggcctt	540
gtgtctttcg	gaaaagcccc	gtgtggccaa	cttggcgtgc	cagggtgtcta	caccaacctc	600
tgcaaatcca	ctgagtggat	agagaaaacc	gtccagncca	gttaactctg	gggactggga	660
acccatgaaa	ttgaccccca	aatacatcct	gcggaangaa	ttcaggaata	tctgttccca	720
gcccctcctc	cctcaggccc	aggagtccag	gccccagcc	cctcctccct	caaaccagg	780
gtacagatcc	ccagccctc	ctccctcaga	cccaggagtc	cagaccccc	agccctcnt	840
ccntcagacc	caggagtcca	gcccctcctc	cntcagacgc	aggagtccag	acccccagc	900

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ccntcntccg tcagaccagc ggggtgcaggc ccccaacccc tcntccntca gagtcagagg 960
tccaagcccc caaccctctg ttccccagac ccagagggtnc aggtcccagc ccctcctccc 1020
tcagaccagc cggccaatg ccacctagan tntccctgta cacagtgcgc ccttggtggca 1080
ngttgaccca acctaccag ttggttttgc attttttgc cctttcccct agatccagaa 1140
ataaagtnta agagaagcgc aaaaaaa 1167

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```

<210> 176
<211> 205
<212> PRT
<213> Homo sapien

```

```

<220>
<221> VARIANT
<222> (1)...(205)
<223> Xaa = Any Amino Acid

```

```

<400> 176
Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp
1 5 10 15
Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu
20 25 30
Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val
35 40 45
Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Leu Leu Leu
50 55 60
Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser
65 70 75 80
Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly
85 90 95
Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg Met
100 105 110
Pro Thr Val Leu His Cys Val Asn Val Ser Val Val Ser Glu Xaa Val
115 120 125
Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys Ala
130 135 140
Gly Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly Gly
145 150 155 160
Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly Lys
165 170 175
Ala Pro Cys Gly Gln Leu Gly Val Pro Gly Val Tyr Thr Asn Leu Cys
180 185 190
Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Xaa Ser
195 200 205

```

```

<210> 177
<211> 1119
<212> DNA
<213> Homo sapien

```

```

<400> 177
gcgcactcgc agccctggca ggcggcactg gtcattgaaa acgaattgtt ctgctcgggc 60
gtcctgggtgc atccgcagtg ggtgctgtca gccgcacact gtttccagaa ctctacacc 120
atcgggcttg gcctgcacag tcttgaggcc gaccaagagc caggagacca gatgggtggag 180
gccagcctct ccgtacggca cccagagtac aacagaccct tgctcgctaa cgacctcatg 240
ctcatcaagt tggacgaatc cgtgtccgag tctgacacca tccggagcat cagcattgct 300
tcgcagtgcc ctacgcggg gaactottgc ctcgtttctg gctggggctc gctggcgaaac 360
gatgctgtga ttgccatcca gtcccagact gtgggaggct gggagtgtga gaagctttcc 420
caaccctggc agggttgtac catttcggca acttccagtg caaggacgtc ctgctgcac 480

```

```

ctcactgggt gctcactact gctcactgca tcacccggaa cactgtgac aactagccag 540
caccatagtt ctccgaagtc agactatcat gattactgtg ttgactgtgc tgtctattgt 600
actaaccatg ccgatgttta ggtgaaatta gcgtcacttg gcctcaacca tcttggtatc 660
cagttatcct cactgaattg agatttcctg cttcagtgtc agccattccc acataatttc 720
tgacctacag aggtgagga tcatatagct cttcaaggat gctgggtactc ccctcacaaa 780
ttcattttctc ctggtttagt gaaaggtgcg ccctctggag cctcccaggg tgggtgtgca 840
ggtcacaatg atgaatgtat gatcgtgttc ccattaccca aagcctttaa atccctcatg 900
ctcagtacac cagggcaggt ctagcatttc ttcatttagt gtatgctgtc cattcatgca 960
accacctcag gactcctgga ttctctgcct agttgagctc ctgcatgctg cctccttggg 1020
gaggtgaggg agagggccca tggttcaatg ggatctgtgc agttgtaaca cattaggtgc 1080
ttaataaaca gaagctgtga tgttaaaaaa aaaaaaaaa 1119

```

&lt;210&gt; 178

&lt;211&gt; 164

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; VARIANT

&lt;222&gt; (1)...(164)

&lt;223&gt; Xaa = Any Amino Acid

&lt;400&gt; 178

```

Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp
 1      5      10      15
Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu
      20      25      30
Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val
      35      40      45
Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu Leu
      50      55      60
Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser
      65      70      75      80
Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly
      85      90      95
Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Asp Ala Val
      100     105     110
Ile Ala Ile Gln Ser Xaa Thr Val Gly Gly Trp Glu Cys Glu Lys Leu
      115     120     125
Ser Gln Pro Trp Gln Gly Cys Thr Ile Ser Ala Thr Ser Ser Ala Arg
      130     135     140
Thr Ser Cys Cys Ile Leu Thr Gly Cys Ser Leu Leu Leu Thr Ala Ser
      145     150     155     160
Pro Gly Thr Leu

```

&lt;210&gt; 179

&lt;211&gt; 250

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 179

```

ctggagtgcc ttggtgtttc aagcccctgc aggaagcaga atgcaccttc tgaggcacct 60
ccagctgccc ccggccgggg gatgcgaggg tcggagcacc cttgcccggc tgtgattgct 120
gccaggcaact gttcatctca gcttttctgt ccctttgctc ccggcaagcg cttctgctga 180
aagttcatat ctggagcctg atgtcttaac gaataaaggt cccatgctcc acccgaaaaa 240
aaaaaaaaa 250

```



64

<210> 180  
 <211> 202  
 <212> DNA  
 <213> Homo sapien

<400> 180  
 actagtccag tgtggtggaa ttccattgtg ttgggcccaa cacaatggct acctttaaca 60  
 tcacccagac cccgcccctg cccgtgcccc acgctgctgc taacgacagt atgatgctta 120  
 ctctgtact cggaactat ttttatgtaa ttaatgtatg ctttcttgtt tataaatgcc 180  
 tgatttaaaa aaaaaaaaaa aa 202

<210> 181  
 <211> 558  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(558)  
 <223> n = A,T,C or G

<400> 181  
 tccytttgkt naggtttkkg agacamccck agacctwaan ctgtgtcaca gacttcyngg 60  
 aatgttttagg cagtgttagt aatttcytcg taatgattct gttattactt tcctnattct 120  
 ttattcctct ttcttctgaa gattaatgaa gttgaaaatt gaggtggata aatacaaaaa 180  
 ggtagtgtga tagtataagt atctaagtgc agatgaaagt gtgttatata tatccattca 240  
 aaattatgca agttagtaat tactcagggt taactaaatt actttaatat gctgttgaac 300  
 ctactctgtt ccttggctag aaaaaattat aaacaggact ttgttagttt ggggaagccaa 360  
 attgataata ttctatgttc taaaagttgg gctatacata aattattaag aaatatggaw 420  
 ttttattccc aggaatatgg kgttcatttt atgaatatta cscrggatag awgtwtgagt 480  
 aaaaacagtt ttggtwaata ygtwaatatg tcmtaaataa acaakgcttt gacttatttc 540  
 caaaaaaaaa aaaaaaaaaa 558

<210> 182  
 <211> 479  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(479)  
 <223> n = A,T,C or G

<400> 182  
 acagggwttk grgatgcta agscccorga rwtggtttga tccaacctg gcttwttttc 60  
 agaggggaaa atggggccta gaagttacag mscatytagy tgggtgcgmg gcacccctgg 120  
 cstcacacag astcccgagt agctgggact acaggcacac agtcactgaa gcaggccctg 180  
 ttwgcaattc acgttgccac ctccaactta aacattcttc atatgtgatg tccttagtca 240  
 ctaagggttaa actttcccac ccagaaaagg caacttagat aaaatcttag agtactttca 300  
 tactmttcta agtcctcttc cagcctcact kkgagtcctm cytggggggt gataggaant 360  
 ntctcttggc tttctcaata aartctctat ycatctcatg ttaatttgg tacgcata 420  
 awtgstgara aaattaaaat gttctgggty mactttaaaa aaaaaaaaaa aaaaaaaaaa 479

<210> 183  
 <211> 384  
 <212> DNA  
 <213> Homo sapien

65

<400> 183  
 aggcgggagc agaagctaaa gccaaagccc aagaagagtg gcagtgccag cactgggtgcc 60  
 agtaccagta ccaataacag tgccagtgcc agtgccagca ccagtgggtg ctccagtgc 120  
 ggtgccagcc tgaccgccac tctcacattt gggtctctcg ctggccttgg tggagctggt 180  
 gccagcacca gtggcagctc tgggtgcctgt ggtttctcct acaagtgaga ttttagatat 240  
 tgtaaatcct gccagtcttt ctcttcaagc caggggtgcat cctcagaaac ctactcaaca 300  
 cagcactcta ggcagccact atcaatcaat tgaagttgac actctgcatt aratctattt 360  
 gccatttcaa aaaaaaaaaa aaaa 384

&lt;210&gt; 184

&lt;211&gt; 496

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(496)

&lt;223&gt; n = A,T,C or G

<400> 184  
 accgaattgg gaccgctggc ttataagcga tcatgttynt ccrgtatcac ctcaacgagc 60  
 agggagatcg agtctatacg ctgaagaaat ttgaccgat gggacaacag acctgctcag 120  
 cccatcctgc tcggttctcc ccagatgaca aatactctsg acaccgaatc accatcaaga 180  
 aacgcttcaa ggtgctcatg acccagcaac cgcgccctgt cctctgaggg tcccttaaac 240  
 tgatgtcttt tctgccacct gttacccctc ggagactccg taaccaaact ctccgactg 300  
 tgagccctga tgcccttttg ccagccatac tctttggcat ccagtctctc gtggcgattg 360  
 attatgcttg tgtgaggcaa tcatggtggc atcacccata aagggaacac atttgacttt 420  
 tttttctcat attttaaatt actacmagaw tattwmagaw waaatgawtt gaaaaactst 480  
 taaaaaaaaa aaaaaa 496

&lt;210&gt; 185

&lt;211&gt; 384

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

<400> 185  
 gctggtagcc tatggcgkgg cccacggagg ggctcctgag gccacggrac agtgacttcc 60  
 caagtatcyt ggcsgcgtc ttctaccgtc cctacctgca gatcttcggg cagattcccc 120  
 aggaggacat ggacgtggcc ctcatggagc acagcaactg ytcgtcggag cccggcttct 180  
 gggcacaccc tcctggggcc caggcgggca cctgcgtctc ccagtatgcc aactggctgg 240  
 tggtgctgct cctcgtcatc ttcctgctcg tggccaacat cctgctggtc aacttgctca 300  
 ttgccatgtt cagttacaca ttcggcaaaag tacagggcaa cagcgatctc tactgggaag 360  
 gcgcagcgtt accgcctcat ccgg 384

&lt;210&gt; 186

&lt;211&gt; 577

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(577)

&lt;223&gt; n = A,T,C or G

<400> 186  
 gagttagctc ctccacaacc ttgatgaggt cgtctgcagt ggcctctcgc ttcataccgc 60  
 tnccatcgct atactgtagg tttgccacca cytcctggca tcttggggcg gcntaatatt 120  
 ccaggaaact ctcaatcaag tcaccgtcga tgaaacctgt gggctgggtc tgtcttcgcg 180

66

tgggtgtgaa	aggatctccc	agaaggagtg	ctcgatcttc	cccacacttt	tgatgacttt	240
attgagtcga	ttctgcatgt	ccagcaggag	gttgtagcag	ctctctgaca	gtgaggtcac	300
cagccctatc	atgccgttga	mcgtgccgaa	garcaccgag	ccttgtgtgg	gggkkgaggt	360
ctcaccacga	ttctgcatta	ccagagagcc	gtggcaaaaag	acattgacaa	actcgcgccag	420
gtggaaaaaag	amcamctcct	ggargtgctn	gccgctcctc	gtcmgttggt	ggcagcgctw	480
tccttttgac	acacaaaaca	gttaaaggca	ttttcagccc	ccagaaaantt	gtcatcatcc	540
aagatntcgc	acagcactna	tccagttggg	attaaat			577

<210> 187  
 <211> 534  
 <212> DNA  
 <213> Homo sapien  
  
 <220>  
 <221> misc\_feature  
 <222> (1)...(534)  
 <223> n = A,T,C or G

aacatcttcc	tgtataatgc	tgtgtaatat	cgatccgatn	ttgtctgstg	agaatycatw	60
actkggaaaa	gmaacattaa	agcctggaca	ctggtattaa	aattcacaaat	atgcaacact	120
ttaaacagtg	tgtcaatctg	ctcccyynac	tttgtcoatca	ccagtctggg	aakaagggta	180
tgcctatttc	acacctgtta	aaagggcgct	aagcattttt	gattcaacat	cttttttttt	240
gacacaagtc	cgaaaaaagc	aaaagtaaac	agttatyaat	ttgttagcca	attcactttc	300
ttcatgggac	agagccatyt	gatttaaaaa	gcaaattgca	taatattgag	cttygggagc	360
tgatatttga	gcggaagagt	agcctttcta	cttcaccaga	cacaactccc	tttcatattg	420
ggatgttnac	naaagtwatg	tctctwacag	atgggatgct	tttgtggcaa	ttctgttctg	480
aggatctccc	agtttattta	ccacttgcac	aagaaggcgt	tttcttctc	aggc	534

<210> 188  
 <211> 761  
 <212> DNA  
 <213> Homo sapien  
  
 <220>  
 <221> misc\_feature  
 <222> (1)...(761)  
 <223> n = A,T,C or G

agaaaccagt	atctctnaaa	acaacctctc	ataccttggt	gacctaat	ttgtgtgcgtg	60
tgtgtgtgcg	cgcataattat	atagacaggc	acatcttttt	tacttttgta	aaagcttatg	120
cctcttttgg	atctatatct	gtgaaagttt	taatgatctg	ccataatgtc	ttggggacct	180
ttgtcttctg	tgtaaattggt	actagagaaa	acacctatnt	tatgagtcaa	tctagttngt	240
tttattcgac	atgaaggaaa	ttccagatn	acaacactna	caaaactctcc	ctkgackarg	300
ggggacaaaag	aaaagcaaaa	ctgamcataa	raaacaatwa	cctggtgaga	arttgcataa	360
acagaaatwr	ggtagtatat	tgaarnacag	catcattaaa	rmgttwtktt	wttctccctt	420
gcaaaaaaca	tgtacngact	tcccgttgag	taatgccaag	ttgttttttt	tatnataaaa	480
cttgcccttc	attacatggt	tnaaagtggg	gtggtgggccc	aaaatattga	aatgatggaa	540
ctgactgata	aagctgtaca	aataagcagt	gtgcctaaca	agcaacacag	taatgttgac	600
atgcttaatt	cacaaatgct	aatttcatta	taaatgtttg	ctaaaataca	ctttgaacta	660
tttttctgt	ttcccagagc	tgagatntta	gattttatgt	agtatnaagt	gaaaaantac	720
gaaaataata	acattgaaga	aaaananaaa	aaanaaaaaa	a		761

<210> 189  
 <211> 482  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(482)  
 <223> n = A,T,C or G

<400> 189  
 tttttttttt tttgccgatn ctactatttt attgcaggan gtgggggtgt atgcaccgca 60  
 caccggggct atnagaagca agaaggaagg agggagggca cagccccttg ctgagcaaca 120  
 aagccgcctg ctgccttctc tgtctgtctc ctggtgcagg cacatgggga gaccttcccc 180  
 aaggcagggg ccaccagtcc aggggtggga atacaggggg tgggangtgt gcataagaag 240  
 tgataggcac aggccacccg gtacagacc ctcggctcct gacaggtna tttcgaccag 300  
 gtcattgtgc cctgcccagg cacagcgtan atctggaaaa gacagaatgc tttccttttc 360  
 aaatttggct ngtcattngaa ngggcanttt tccaanttng gctnnggtctt ggtacncttg 420  
 gttcggccca gctccnctgc caaaaantat tcaccennct ccnaattgct tgcnggnccc 480  
 cc 482

<210> 190  
 <211> 471  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(471)  
 <223> n = A,T,C or G

<400> 190  
 tttttttttt ttttfaaaaca gtttttcaca acaaaattta ttagaagaat agtggttttg 60  
 aaaactctcg catccagtga gaactacat acaccacatt acagctnnga atgtntctca 120  
 aatgtctggg caaatgatac aatggaacca ttcaatctta cacatgcacg aaagaacaag 180  
 cgcttttgac atacaatgca caaaaaaaaa aggggggggg gaccacatgg attaaaattt 240  
 taagtactca tcacatacat taagacacag ttctagtcca gtcnaaaatc agaactgcnt 300  
 tgaaaaaattt catgtatgca atccaaccaa agaacttnat tggatgatcat gantnctcta 360  
 ctacatcnac cttgatcatt gccaggaacn aaaagttnaa ancacnngt acaaaaaanaa 420  
 tctgtaattn anttcaacct ccgtacngaa aaatnttntt tatacactcc c 471

<210> 191  
 <211> 402  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(402)  
 <223> n = A,T,C or G

<400> 191  
 gagggattga aggtctgttc tastgtcggm ctgttcagcc accaactcta acaagttgct 60  
 gtcttccact cactgtctgt aagcttttta acccagacwg tatcttcata aatagaacaa 120  
 attcttcacc agtcacatct tctaggacct ttttggtatc agttagtata agctcttcca 180  
 ctctctttgt taagacttca tctggtaaag tcttaagttt tgtagaaagg aattyaattg 240  
 ctcgttctct aacaatgtcc tctccttgaa gtatttggct gaacaaccca cctaaagtcc 300  
 ctttgtgcat ccattttaaa tatacttaat agggcattgk tncaactagg taaattctgc 360  
 aagagtcate tgtctgcaaa agttgcgtta gtatactctgc ca 402

<210> 192  
 <211> 601

<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(601)  
<223> n = A,T,C or G

<400> 192  
gagctcggat ccaataatct ttgtctgagg gcagcacaca tatncagtgc catggnaact 60  
ggtctacccc acatgggagc agcatgccgt agntatataa ggctattccc tgagtcagac 120  
atgcytyttt gaytaccgtg tgccaagtgc tgggtattct yaacacacyt ccatcccgyt 180  
cttttggtga aaaactggca cttktctgga actagcarga catcacttac aaattcaccc 240  
acgagacact tgaaagggtg aacaaagcga ytcctgcatt gctttttgtc cctccggcac 300  
cagttgtcaa tactaaccog ctggtttgcc tccatcacat ttgtgatctg tagctctgga 360  
tacatctcct gacagtactg aagaacttct tcttttgttt caaaagcarg tcttggtgcc 420  
tgttgatca ggttcccatt tcccagtcyg aatgttcaca tggcatattt wacttcccac 480  
aaaacattgc gatttgaggc tcagcaacag caaatcctgt tccggcattg gctgcaagag 540  
cctcgatgta gccggccagc gccaaaggcag gcgccgtgag ccccaccagc agcagaagca 600  
g 601

<210> 193  
<211> 608  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(608)  
<223> n = A,T,C or G

<400> 193  
atacagccca natcccacca cgaagatgog cttgttgact gagaacctga tgcggtcact 60  
ggtcccogctg tagccccagc gactctccac ctgctggaag cggttgatgc tgcactcytt 120  
cccaacgcag gcagmagcgg gscgggtcaa tgaactccay tcgtggcttg gggtkgacgg 180  
tkaagtgcag gaagaggctg accacctogc ggtccaccag gatgcccagc tgtgcgggac 240  
ctgcagcgaa actcctcgat ggtcatgagc gggaagcgaa tgaggcccag ggccttgccc 300  
agaaccttcc gcctgttctc tggcgctacc tgcagctgct gccgctgaca ctcggcctog 360  
gaccagcgga caaacggcrt tgaacagccg cactcacgg atgccagtg tgcgcgcctc 420  
caggammgsc accagcgtgt ccaggtcaat gtcggtgaag ccctccgcgg gtrattggct 480  
ctgcagtgtt tttgtcgatg ttctccaggc acaggtggc cagctgcggg tcatcgaaga 540  
gtcgcgcctg cgtgagcagc atgaaggcgt tgcgggctcg cagttcttct tcaggaaactc 600  
cacgcaat 608

<210> 194  
<211> 392  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(392)  
<223> n = A,T,C or G

<400> 194  
gaacggctgg accttgccctc gcattgtgct tgctggcagg gaataccttg gcaagcagyt 60  
ccagtccgag cagccccaga ccgctgccgc ccgaagctaa gcctgcctct ggccttcccc 120  
tccgcctcaa tgagaacca gtagtgggag cactgtgttt agagttaaga gtgaacactg 180

tttgatttta	ottgggaatt	tcctctgtta	tatagctttt	cccaatgcta	atttccaaac	240
aacaacaaca	aaataacatg	tttgcctgtt	aagttgtata	aaagtaggtg	attctgtatt	300
taaagaaaat	attactgtta	catatactgc	ttgcaatttc	tgtattttatt	gktnctstgg	360
aaataaatat	agttattaaa	ggttgtcant	cc			392

&lt;210&gt; 195

&lt;211&gt; 502

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(502)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 195

ccsttkgagg	ggtkaggkyc	cagttyccga	gtggaagaaa	caggccagga	gaagtgcgtg	60
ccgagctgag	gcagatgttc	ccacagtgc	ccccagagcc	stgggstata	gtytctgacc	120
cctcncaagy	aaagaccacs	ttctggggac	atgggctgga	gggcaggacc	tagaggcacc	180
aagggaagyc	ccatttccgg	ggstgttccc	cgaggaggaa	gggaaggggc	totgtgtgcc	240
ccccasgagg	aagaggccct	gagtcctggg	atcagacacc	ccttcacgtg	tatccccaca	300
caaatgcaag	ctcaccaagg	tcccctctca	gtccccttcc	stacaccctg	amcggccact	360
gscscacacc	caccagagc	acgccacccg	ccatggggar	tgtgctcaag	gartcgcnng	420
gcarcgtgga	catctngtcc	cagaaggggg	cagaatctcc	aatagangga	ctgarcmstt	480
gctnanaaaa	aaaaanaaaa	aa				502

&lt;210&gt; 196

&lt;211&gt; 665

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(665)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 196

ggttacttg	tttcattgcc	accacttagt	ggatgtcatt	tagaaccatt	ttgtctgctc	60
cctctggaag	ccttgccgag	agcggacttt	gtaattgttg	gagaataact	gctgaatttt	120
wagctgtttk	gagttgatts	gcaccactgc	accacaact	tcaatatgaa	aacyawttga	180
actwatattat	tatcttgtga	aaagtataac	aatgaaaatt	ttgttcatac	tgtattkatc	240
aagtatgatg	aaaagcaawa	gatatatatt	cttttattat	gttaaattat	gattgccatt	300
attaatcggc	aaaatgtgga	gtgtatgttc	ttttcacagt	aatatatgcc	ttttgtaact	360
tcacttggtt	attttattgt	aaatgartta	caaaattctt	aatttaagar	aatggatgtg	420
watatttatt	tcattaattt	ctttcctkgt	ttacgtwaat	tttgaaaaga	wtgcatgatt	480
tcttgacaga	aatcgatctt	gatgctgtgg	aagtagtttg	accacatcc	ctatgagttt	540
ttcttagaat	gtataaaggt	tgtagcccat	cnaacttcaa	agaaaaaat	gaccacatac	600
tttgcaatca	ggctgaaatg	tggcatgctn	ttctaattcc	aactttataa	actagcaaan	660
aagtg						665

&lt;210&gt; 197

&lt;211&gt; 492

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(492)

<223> n = A,T,C or G

<400> 197

tttntttttt	ttttttttgc	aggaaggatt	ccattttattg	tggatgcatt	ttcacaatat	60
atgtttattg	gagcgatcca	ttatcagtga	aaagtatcaa	gtgtttataa	natttttagg	120
aaggcagatt	cacagaacat	gctngtcngc	ttgcagtttt	acctcgtana	gatnacagag	180
aattatagtc	naaccagtaa	acnaggaatt	tacttttcaa	aagattaaat	ccaaactgaa	240
caaaattcta	ccctgaaact	tactccatcc	aaatattgga	ataanagtca	gcagtgatac	300
attctcttct	gaactttaga	ttttctagaa	aaatatgtaa	tagtgatcag	gaagagctct	360
tgttcaaaag	tacaacnaag	caatgttccc	ttaccatagg	ccttaattca	aactttgatc	420
catttcactc	ccatcacggg	agtcaatgct	acctgggaca	cttgatattt	gttcatnctg	480
ancntggctt	aa					492

<210> 198

<211> 478

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(478)

<223> n = A,T,C or G

<400> 198

tttnttttgn	atttcantct	gtannaanta	ttttcattat	gtttattana	aaaatatnaa	60
tgnttccacn	acaaatcatn	ttacntnagt	aagaggccan	ctacattgta	caacatacac	120
tgagtatatt	ttgaaaagga	caagttttaa	gtanaacncat	attgccganc	atancacatt	180
tatacatggc	ttgattgata	tttagcacag	canaaactga	gtgagttacc	agaaanaaat	240
natatatgtc	aatcngattt	aagatacaaa	acagatccta	tggtagatan	catcntgtag	300
gagttgtggc	tttatgttta	ctgaaagtca	atgcagttcc	tgtacaaaga	gatggccgta	360
agcattctag	tacctctact	ccatgggtta	gaatcgtaca	cttatgttta	catatgtnca	420
gggtaagaat	tgtgttaagt	naanttatgg	agaggtccan	gagaaaaatt	tgatncaa	478

<210> 199

<211> 482

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(482)

<223> n = A,T,C or G

<400> 199

agtgacttgt	cctccaacaa	aacccttga	tcaagtttgt	ggcactgaca	atcagaccta	60
tgctagtcc	tgcatctat	tcgctactaa	atgcagactg	gaggggacca	aaaaggggca	120
tcaactccag	ctggattatt	ttggagcctg	caaatctatt	cctacttgta	cggactttga	180
agtgattcag	tttcctctac	ggatgagaga	ctggctcaag	aatatcctca	tgcagcttta	240
tgaagccnac	tctgaacacg	ctggttatct	nagatgagaa	ncagagaaat	aaagtcnaga	300
aaatttacct	ggangaaaag	aggcttngg	ctggggacca	tcccattgaa	ccttctctta	360
anggacttta	agaanaaaact	accacatgtn	tgtngtatcc	tgggtgccngg	ccgtttantg	420
aacntngacn	ncacccttnt	ggaatanant	cttgacngcn	tcctgaactt	gctcctctgc	480
ga						482

<210> 200

<211> 270

<212> DNA

<213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(270)  
 <223> n = A,T,C or G

<400> 200  
 cgccgcgaag tgcaactcca gctggggccg tgcggacgaa gattctgcc a gcagttggtc 60  
 cgactgcgac gacggcgccg gcgacagtcg caggtgcagc gcgggcgcct ggggtcttgc 120  
 aaggetgagc tgacgccgca gaggtcgtgt cacgtccac gaccttgacg ccgtcgggga 180  
 cagccggaac agagcccggg gaangcggga ggcctcgggg agcccctcgg gaaggcgccg 240  
 ccgagagata cgcaggtgca ggtggccgcc 270

<210> 201  
 <211> 419  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(419)  
 <223> n = A,T,C or G

<400> 201  
 tttttttttt ttttggaaatc tactgcgagc acagcaggtc agcaacaagt ttattttgca 60  
 gctagcaagg taacagggtg gggcatggtt acatgttcag gtcaacttcc tttgtcgtgg 120  
 ttgattggtt tgtcttttatg gggcgccggg ggggtagggg aaancgaagc anaantaaca 180  
 tggagtgggt gcaccctccc tgtagaacct gggttacnaaa gcttggggca gttcacctgg 240  
 tctgtgaccg tcattttctt gacatcaatg ttattagaag tcaggatata ttttagagag 300  
 tccactgtnt ctggaggagg attagggttt cttgccaana tccaancaa atccacntga 360  
 aaaagttgga tgatncangt acngaatacc ganggcatan ttctcatant cggtggcca 419

<210> 202  
 <211> 509  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(509)  
 <223> n = A,T,C or G

<400> 202  
 tttntttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 60  
 tggcacttaa tccattttta tttcaaaatg tctacaaant ttnaatncnc cattatacng 120  
 gtnattttnc aaaatctaaa nnttattcaa atntnagcca aantccttac ncaaattnaa 180  
 tacnncnaaa aatcaaaaat ataentntct ttcagcaaac ttngttacat aaattaaaaa 240  
 aatatatacg gctgggtggt tcaaagtaca attatcttaa cactgcaaac atnttttnaa 300  
 ggaactaaaa taataaaaaa cactnccgca aagggttaaag ggaacaacaa attcntttta 360  
 caacancnnc nattataaaa atcatatctc aaatccttagg ggaatatata cttcacacng 420  
 ggatcttaac ttttactnca ctttgtttat ttttttanaa ccattgtntt gggcccaaca 480  
 caatggnaat ncncncncnc tggactagt 509

<210> 203  
 <211> 583  
 <212> DNA  
 <213> Homo sapien



<220>  
 <221> misc\_feature  
 <222> (1)...(583)  
 <223> n = A,T,C or G

<400> 203  
 tttttttttt ttttttttga cccccctctt ataaaaaaca agttaccatt ttatttttact 60  
 tacacatatatt ttttttataa ttggtatttag atattcaaaa ggcagctttt aaaatcaaac 120  
 taaatggaaa ctgccttaga tacataattc ttaggaatta gcttaaaatc tgcctaaagt 180  
 gaaaatcttc tctagctctt ttgactgtaa atttttgact cttgtaaaac atccaaattc 240  
 atttttcttg tctttaaaat tatctaattc ttccattttt tccctattcc aagtcaattt 300  
 gcttctctag cctcatttcc tagctcttat ctactattag taagtggctt ttttcctaaa 360  
 agggaaaaca ggaagagana atggcacaca aaacaaacat tttatattca tatttctacc 420  
 tacgttaata aaatagcatt ttgtgaagcc agctcaaaag aaggcttaga tccttttatg 480  
 tccatttttag tcaactaaacg atatcnaaag tgccagaatg caaaagggtt gtgaacattt 540  
 attcaaaagc taatataaga tatttcacat actcatctt ctg 583

<210> 204  
 <211> 589  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(589)  
 <223> n = A,T,C or G

<400> 204  
 ttttttttnt tttttttttt ttttttntct ttcttttttt ttganaatga ggatcgagtt 60  
 tttcactctc tagatagggc atgaagaaaa ctcatctttc cagcttttaa ataacaatca 120  
 aatctcttat gctatatcat attttaagtt aaactaatga gtcactggct tatcttctcc 180  
 tgaaggaaat ctgttcattc ttctcattca tatagttata tcaagtacta ccttgcatat 240  
 tgagagggtt ttcttctcta tttacacata tttttccatg tgaatttgta tcaaaccctt 300  
 attttcatgc aaactagaaa ataatgtntt cttttgcata agagaagaga acaatatnag 360  
 cattacaaaa ctgctcaaat tgtttggtta gnttatccat tataattagt tnggcaggag 420  
 ctaatacaaa tcacattttac ngacnagcaa taataaaact gaagtaccag ttaaatatcc 480  
 aaaataatta aaggaacatt tttagcctgg gtataattag ctaattcact ttacaagcat 540  
 ttattnagaa tgaattcaca tgttattatt ccntagccca acacaatgg 589

<210> 205  
 <211> 545  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(545)  
 <223> n = A,T,C or G

<400> 205  
 tttttntttt ttttttcagt aataatcaga acaatattta tttttatatt taaaattcat 60  
 agaaaagtgc cttacattta ataaaagttt gtttctcaaa gtgatcagag gaattagata 120  
 tngtcttgaa caccaatatt aatttgagga aaatacacca aaatacatta agtaaattat 180  
 ttaagatcat agagcttgta agtgaaaaga taaaatttga cctcagaaac tctgagcatt 240  
 aaaaatccac tattagcaaa taaattacta tggacttctt gctttaattt tgtgatgaat 300  
 atgggggtgc actggtaaac caacacattc tgaaggatac attacttagt gatagattct 360  
 tatgtacttt gctanatnac gtggatatga gttgacaagt ttctctttct tcaatctttt 420  
 aaggggcnga ngaaatgagg aagaaaagaa aaggattacg catactgttc tttctatngg 480

aaggattaga tatgtttcct ttgccaatat taaaaaata ataatgttta ctactagtga 540  
aacc 545

<210> 206  
<211> 487  
<212> DNA  
<213> Homo sapien  
  
<220>  
<221> misc\_feature  
<222> (1)...(487)  
<223> n = A,T,C or G

<400> 206  
tttttttttt ttttttagtc aagtttctna tttttattat aattaaagtc ttgggtcattt 60  
catttattag ctctgcaact tacatattta aattaaagaa acgttnttag acaactgtna 120  
caatttataa atgtaagggt ccattattga gtanatatat tcctccaaga gtggatgtgt 180  
cccttctccc accaactaat gaancagcaa cattagttaa attttattag tagatnatac 240  
actgctgcaa acgctaattc tcttctccat ccccatgtng atattgtgta tatgtgtgag 300  
ttggttagaa tgcatacanca atctnacaat caacagcaag atgaagctag gcntgggctt 360  
tcggtgaaaa tagactgtgt ctgtctgaat caaatgatct gacctatcct cgggtggcaag 420  
aactcttcga accgcttcct caaaggcngc tgccacattt gtggcntctn ttgcacttgt 480  
ttcaaaa 487

<210> 207  
<211> 332  
<212> DNA  
<213> Homo sapien  
  
<220>  
<221> misc\_feature  
<222> (1)...(332)  
<223> n = A,T,C or G

<400> 207  
tgaattggct aaaagactgc atttttanaa ctagcaactc ttatttcttt cctttaaaaa 60  
tacatagcat taaatcccaa atcctattta aagacctgac agcttgagaa ggtcactact 120  
gcatttatag gaccttctgg tggttctgct gttacntttg aantctgaca atccttgana 180  
atctttgcat gcagaggagg taaaaggat tggattttca cagaggana acacagcgca 240  
gaaatgaagg ggccaggctt actgagcttg tccactggag ggctcatggg tgggacatgg 300  
aaaagaaggc agcctaggcc ctggggagcc ca 332

<210> 208  
<211> 524  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(524)  
<223> n = A,T,C or G

<400> 208  
agggcgtggt gcggaggggc ttactgtttt gtctcagtaa caataaatac aaaaagactg 60  
gttggtgtcc ggcccatcc aaccacgaag ttgatttctc ttgtgtgcag agtgactgat 120  
tttaaaggac atggagcttg tcacaatgtc acaatgtcac agtgtgaagg gcacactcac 180  
tcccgcgtga ttacatttta gcaaccaaca atagctcatg agtccatact tgtaaatact 240  
tttggcagaa tacttnttga aacttgcaga tgataactaa gatccaagat atttcccaaa 300

gtaaatagaa gtgggtcata atattaatta cctgttcaca tcagcttcca tttacaagtc	360
atgagcccag acactgacat caaactaagc ccacttagac tcctcaccac cagtctgtcc	420
tgtcatcaga caggaggctg tcaccttgac caaattctca ccagtcaatc atctatccaa	480
aaaccattac ctgatccact tccggtaatg caccaccttg gtga	524

<210> 209  
 <211> 159  
 <212> DNA  
 <213> Homo sapien

<400> 209	
gggtgaggaa atccagagtt gccatggaga aaattccagt gtcagcattc ttgctccttg	60
tggccctctc ctacactctg gccagagata ccacagtcaa acctggagcc aaaaaggaca	120
caaaggactc tcgacccaaa ctgcccacaga cctcttcca	159

<210> 210  
 <211> 256  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(256)  
 <223> n = A,T,C or G

<400> 210	
actccctggc agacaaaggc agaggagaga gctctgttag ttctgtgttg ttgaactgcc	60
actgaatttc ttccacttg gactattaca tgccantga gggactaatg gaaaaacgta	120
tggggagatt ttanccaatt tangtntgta aatggggaga ctggggcagg cgggagagat	180
ttgcagggtg naaatgggan ggctggtttg ttanatgaac agggacatag gaggtaggca	240
ccaggatgct aaatca	256

<210> 211  
 <211> 264  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(264)  
 <223> n = A,T,C or G

<400> 211	
acattgtttt tttagataa agcattgaga gagctctcct taacgtgaca caatggaagg	60
actggaacac ataccacat cttgtttctg agggataatt ttctgataaa gtcttgctgt	120
atattcaagc acatatgtta tatattatc agttccatgt ttatagccta gttaaggaga	180
ggggagatac attcngaaag aggactgaaa gaaatactca agtnggaaaa cagaaaaaga	240
aaaaaaggag caaatgagaa gcct	264

<210> 212  
 <211> 328  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(328)  
 <223> n = A,T,C or G

<400> 212  
 acccaaaaat ccaatgctga atatttggct tcattattcc canattcttt gattgtcaaa 60  
 ggattttaatg ttgtctcagc ttgggcaçtt cagttaggac ctaaggatgc cagccggcag 120  
 gtttatatat gcagcaacaa tattcaagcg cgacaacagg ttattgaact tgcccgccag 180  
 ttnaatttca ttcccattga cttgggatcc ttatcatcag ccagagagat tgaaaattta 240  
 cccctacnac tctttactct ctgganaggg ccagtgggtg tagctataag cttggccaca 300  
 ttttttttct cttttattcct ttgtcaga 328

<210> 213

<211> 250

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(250)

<223> n = A,T,C or G

<400> 213  
 acttatgagc agagcgacat atccnagtgt agactgaata aaactgaatt ctctccagtt 60  
 taaagcattg ctactgaag ggatagaagt gactgccagg agggaaagta agccaaggct 120  
 cattatgcca aagganatat acattttcaat tctccaaact tcttcctcat tccaagagtt 180  
 ttcaatattt gcatgaacct gctgataanc catgttaana aacaaatata tctctnacct 240  
 tctcatcggt 250

<210> 214

<211> 444

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(444)

<223> n = A,T,C or G

<400> 214  
 acccagaatc caatgctgaa tatttggctt cattattccc agattctttg attgtcaaag 60  
 gattttaatgt tgtctcagct tgggcacttc agttaggacc taaggatgcc agccggcagg 120  
 tttatatatg cagcaacaat attcaagcgc gacaacaggc tattgaactt gcccgccagt 180  
 tgaatttcat tcccattgac ttgggatcct tatcatcagc canagagatt gaaaatttac 240  
 ccctacgact ctttactctc tggagagggc cagtgggtgt agctataagc ttggccacat 300  
 ttttttttcc tttattcctt tgtcagagat gcgattcatc catatgctan aaaccaacag 360  
 agtgactttt acaaaattcc tataganatt gtgaataaaa cettacctat agttgccatt 420  
 actttgctct ccctaataata cctc 444

<210> 215

<211> 366

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(366)

<223> n = A,T,C or G

<400> 215  
 acttatgagc agagcgacat atccaagtgt anactgaata aaactgaatt ctctccagtt 60

taaagcattg	ctcactgaag	ggatagaagt	gactgccagg	agggaaagta	agccaaggct	120
cattatgcca	aagganatat	acatttcaat	tctccaaact	tcttcctcat	tccaagagtt	180
ttcaatat	gcatgaacct	gctgataagc	catgttgaga	aacaaatac	tctctgacct	240
tctcatcggt	aagcagaggc	tgtaggcaac	atggaccata	gcgaanaaaa	aacttagtaa	300
tccaagctgt	tttctacact	gtaaccagg	ttccaaccaa	ggtggaaatc	tcctatactt	360
ggtgcc						366

<210> 216  
 <211> 260  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(260)  
 <223> n = A,T,C or G

<400> 216	
ctgtataaac	agaactccac
tgccagggg	agggccgggc
caggagaatc	tccgcttgtc
caagacagg	gcctaaggag
ggtctccaca	ctgctnntaa
gggctnttnc	atctttttat
taataaaaag	tnnaaaaggc
ctcttctcaa	cttttttccc
ttnggctgga	aaatttataa
atcaaaaatt	tcctnaagtt
ntcaagctat	catatatact
ntatcctgaa	aaagcaacat
aattcttcct	tccctccttt

<210> 217  
 <211> 262  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(262)  
 <223> n = A,T,C or G

<400> 217	
acctacgtgg	gtaagtttan
aaatgttata	atttcaggaa
naggaacgca	tataattgta
tcttgccctat	aattttctat
ttaataaagg	aaatagcaaa
ttgggggtggg	gggaatgtag
ggcattctac	agtttgagca
aaatgcaatt	aaatgtggaa
ggacagcact	gaaaaatttt
atgaataatc	tgtatgatta
tatgtctcta	gagtagattt
ataattagcc	acttacccta
atataccttca	tgcttgtaaa
gt	

<210> 218  
 <211> 205  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(205)  
 <223> n = A,T,C or G

<400> 218	
accaaggtgg	tgccattaccg
gaantggatc	aangacacca
tcgtggccaa	cccctgagca
cccctatcaa	ctcccctttt
tagtaaaact	ggaaccttgg
aaatgaccag	gccaagactc
aggcctcccc	agttctactg
acctttgtcc	ttangntna
ngtccagggt	tgctaggaaa
anaaatcagc	agacacagg
gtaaa	

<210> 219

77

<211> 114  
 <212> DNA  
 <213> Homo sapien

<400> 219  
 tactgttttg tctcagtaac aataaatata aaaagactgg ttgtgttccg gcccaccca 60  
 accacgaagt tgatttctct tgtgtgcaga gtgactgatt ttaaaggaca tgga 114

<210> 220  
 <211> 93  
 <212> DNA  
 <213> Homo sapien

<400> 220  
 actagccagc acaaaaggca gggtagcctg aattgctttt tgctctttac atttctttta 60  
 aaataagcat ttagtgctca gtccctactg agt 93

<210> 221  
 <211> 167  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(167)  
 <223> n = A,T,C or G

<400> 221  
 actangtgca ggtgcgacaca aatatttgct gatattccct tcatcttgga ttocatgagg 60  
 tcttttgccc agcctgtggc totactgtag taagtttctg ctgatgagga gccagnatgc 120  
 ccccactac cttccctgac gctccccana aatcacccaa cctctgt 167

<210> 222  
 <211> 351  
 <212> DNA  
 <213> Homo sapien

<400> 222  
 agggcggtgt ggcggaggcg gtactgacct cattagtagg aggatgcatt ctggcacccc 60  
 gttcttcacc tgtcccccaa tccttaaaaag gccatactgc ataaagtcaa caacagataa 120  
 atgtttgtctg aattaaagga tggatgaaaa aaattaataa tgaatttttg cataatccaa 180  
 ttttctcttt tatatttcta gaagaagttt ctttgagcct attagatccc gggaatcttt 240  
 taggtgagca tgattagaga gcttgtagggt tgcttttaca tatatctggc atatttgagt 300  
 ctcgtatcaa aacaatagat tggtaaagggt ggtattattg tattgataag t 351

<210> 223  
 <211> 383  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(383)  
 <223> n = A,T,C or G

<400> 223  
 aaaacaaaca aacaaaaaaa acaattcttc attcagaaaa attatcttag ggactgatat 60  
 tggtaattat ggtcaattta atwrtrttkt ggggcatttc cttacattgt cttgacaaga 120

ttaaaaatgtc	tgtgccaaaa	ttttgtat	tatttggaga	cttcttatca	aaagtaatgc	180
tgccaaagga	agtctaagga	attagtagtg	ttcccmcac	ttgtttggag	tgtgctattc	240
taaaagattt	tgatttcctg	gaatgacaat	tatatittaa	ctttgggtggg	ggaaanagtt	300
ataggaccac	agtcttcact	tctgatactt	gtaaattaat	cttttattgc	acttgttttg	360
accattaagc	tatatgttta	aaa				383

<210> 224  
 <211> 320  
 <212> DNA  
 <213> Homo sapien

ccccgaagg	cttcttgta	gaaaatagta	cagttacaac	caataggaac	aacaaaaaga	60
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tttaractcm	gcattgtgac					320

<210> 225  
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 <212> DNA  
 <213> Homo sapien

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aaaaaaaaaa	aaaa					1214

<210> 226  
 <211> 119  
 <212> DNA  
 <213> Homo sapien

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<210> 227  
 <211> 818

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 227

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tttttgctac	atatggggtc	ccttttcatt	ccttgcaaaa	acactgggtt	ttctgagaac	120
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gcttgctccc	ttccaatcag	ccacttctga	gaacccccat	ctaacttcct	actggaaaag	360
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&lt;210&gt; 228

&lt;211&gt; 744

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 228

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accagattct	aggccagttt	gttccactga	agcttttccc	acagcagtc	acctctgcag	360
gctggcagct	gaatggcttg	cgggtggctc	tgtggcaaga	tcacactgag	atcgatgggt	420
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&lt;210&gt; 229

&lt;211&gt; 300

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 229

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cattacacat	cgaaataaaa	gaaaggtggc	agacttgccc	aacgccaggc	tgacatgtgc	120
tgcagggttg	ttgtttttta	attattattg	ttagaaacgt	caccacacag	ccctgttaat	180
ttgtatgtga	cagccaactc	tgagaaggtc	ctatttttcc	acctgcagag	gatccagtct	240
cactaggctc	ctccttgccc	tcacactgga	gtctccgcca	gtgtgggtgc	ccactgacat	300

&lt;210&gt; 230

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 230

cagcagaaca	aatacaaata	tgaagagtgc	aaagatctca	taaaatctat	gctgaggaat	60
------------	------------	------------	------------	------------	------------	----



gagcgacagt tcaaggagga gaagcttgca gagcagctca agcaagctga ggagctcagg 120  
 caatataaag tcctgggttca cactcaggaa cgagagctga cccagttaag ggagaagttg 180  
 cgggaaggga gagatgcctc cctctcattg aatgagcatc tccaggccct cctcactccg 240  
 gatgaaccgg acaagtccca ggggcaggac ctccaagaaa cagacctcgg ccgcgaccac 300  
 g 301

<210> 231  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 231  
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 ggcaacacgg gactttctcat caggaagtgg gatgtagatg agctgatcaa gacggccagg 180  
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 c 301

<210> 232  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

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 agaagagtcc atctgctgtg aaggagagac agagaactct gggttccgtc gtctgtcca 180  
 cgtgctgtac caagtgtctg tgccagcctg ttacctgttc tctactgaaa tctggctaatt 240  
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 g 301

<210> 233  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 233  
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 cctagaagtt acagagcatc tagctggtgc gctggcaccc ctggcctcac acagactccc 180  
 gagtagctgg gactacaggc acacagtcac tgaagcaggc cctgttagca attctatgcg 240  
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 c 301

<210> 234  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

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 tcaatttcag caacatactt ctcaatttct tcaggattta aaatcttgag ggattgatct 180  
 cgctcatga cagcaagttc aatgtttttg ccacctgact gaaccacttc caggagtgc 240  
 ttgatcacca gcttaatggt cagatcatct gcttcaatgg ctctcgtcagt atagttcttc 300  
 t 301

## 81

<210> 235  
 <211> 283  
 <212> DNA  
 <213> Homo sapien

<400> 235  
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 aattccctca tcttttaggg aatcatttac cagggtttgga gaggattcag acagctcagg 120  
 tgctttcact aatgtctctg aacttctgtc cctctttggt catggatagt ccaataaata 180  
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 ttagggattc aaagaaatat tagatttaag ctcacactgg tca 283

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 <211> 301  
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 <213> Homo sapien

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 tgggtagacg gcttcatgag tacagtgtac tgtggtatcg taatctggac ttgggttgta 240  
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<210> 237  
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 <212> DNA  
 <213> Homo sapien

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 t 301

<210> 238  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 238  
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 accccctgcc tgggaagcag ctccctgggg ggtgggaatg ggtgactaga agggatttca 240  
 gtgtgggacc cagggtctgt tcttcacagt aggaggtgga agggatgact aatttcttta 300  
 t 301

<210> 239  
 <211> 239  
 <212> DNA  
 <213> Homo sapien

<400> 239  
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cataatacct tagagatcaa gaaacattta cacagttcaa ctgtttaaaa atagctcaac	180
attcagccag tgagtagagt gtgaatgcc gcatcacag tatacaggtc cttcaggga	239

<210> 240  
 <211> 300  
 <212> DNA  
 <213> Homo sapien

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gctgggtgag ccagatgact tctgttccct ggtoactttc ttcaatgggg cgaatggggg	180
ctgccagggtt tttaaaatca tgcttcatct tgaagcacac ggtoacttca ccctcctcac	240
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<210> 241  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 241	
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<210> 242  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 242	
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cttaatatca acaaatatat caagcaaact ggaaggcaga ataactacca taatttagta	240
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a	301

<210> 243  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

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<210> 244  
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 <212> DNA

<213> Homo sapien

<400> 244

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ccagggacct	tggaaacagt	tgacactgta	aggtgcttgc	tccccaagac	acatcctaaa	180
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<210> 245

<211> 301

<212> DNA

<213> Homo sapien

<400> 245

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aaggccagga	gatattgtca	ttaatgtara	cttcaggaca	ctagagtata	gcagccctat	180
gttttcaaag	agcagagatg	caattaaata	ttgttttagca	tcaaaaaggc	cactcaatac	240
agctaataaa	atgaaagacc	taattttctaa	agcaattctt	tataatttac	aaagtttttaa	300
g						301

<210> 246

<211> 301

<212> DNA

<213> Homo sapien

<400> 246

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caaatgtgtc	ttacaaaaca	cgttcctaac	aaggatatgct	ttacactacc	aatgcagaaa	300
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<210> 247

<211> 301

<212> DNA

<213> Homo sapien

<400> 247

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a						301

<210> 248

<211> 301

<212> DNA

<213> Homo sapien

<400> 248

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c 301

<210> 249  
<211> 301  
<212> DNA  
<213> Homo sapien

<400> 249  
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ccaggagac acagcagtga ctacagagctg gtcgcacact gtgcctccct cctcaccgcc 180  
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a 301

<210> 250  
<211> 301  
<212> DNA  
<213> Homo sapien

<400> 250  
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cataagcaca tcagtacttt tctctggctg gaatagtaaa cttaaagtatg gtacatctac 180  
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a 301

<210> 251  
<211> 301  
<212> DNA  
<213> Homo sapien

<400> 251  
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c 301

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<211> 301  
<212> DNA  
<213> Homo sapien

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atatatcaag caaactggaa ggcagaataa ctaccataat ttagtataag tacccaaagt 240  
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a 301

<210> 253  
<211> 301  
<212> DNA

<213> Homo sapien

<400> 253

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tggtctgatt	gttttcagac	cttaaaatat	aaacttggtt	cacaagcttt	aatccatgtg	180
gatttttttt	cttagagaac	cacaaaacat	aaaaggagca	agtcggactg	aatacctgtt	240
tccatagtgc	ccacagggta	ttcctcacat	tttctccata	ggaaaatgct	ttttcccaag	300
g						301

<210> 254

<211> 301

<212> DNA

<213> Homo sapien

<400> 254

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ccaaatctct	tcattcttacc	ctgggtggact	cctgactgta	gaattttttg	gttgaaacaa	180
gaaaaaaata	aagcttttga	cttttcaagg	ttgcttaaca	ggtactgaaa	gactggcctc	240
acttaactg	agccaggaaa	agctgcagat	ttattaatgg	gtgtgttagt	gtgcagtgcc	300
t						301

<210> 255

<211> 302

<212> DNA

<213> Homo sapien

<400> 255

agcttttttt	tttttttttt	tttttttttt	ttcattaaaa	aatagtgtc	tttattataa	60
attactgaaa	tgtttctttt	ctgaatataa	atataaatat	gtgcaaagt	tgacttggat	120
tgggattttg	ttgagttctt	caagcatctc	ctaataccct	caagggcctg	agtagggggg	180
aggaaaaagg	actggagggtg	gaatctttat	aaaaaacaag	agtgattgag	gcagattgta	240
aacattatta	aaaaacaaga	aacaaacaaa	aaaatagaga	aaaaaacac	cccaacacac	300
aa						302

<210> 256

<211> 301

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(301)

<223> n = A,T,C or G

<400> 256

gttccagaaa	acattgaagg	tggtctccca	aagtctaact	agggataccc	cctctagcct	60
aggaccctcc	tcccacacc	tcaatccacc	aaaccatcca	taatgcaccc	agataggccc	120
acccccaaaa	gcctggacac	cttgagcaca	cagttatgac	caggacagac	tcattcttat	180
aggcaaatag	ctgctggcaa	actggcatta	cctggtttgt	ggggatgggg	gggcaagtgt	240
gtggcctctc	ggcctgggta	gcaagaacat	tcagggtagg	cctaagttan	tcgtgttagt	300
t						301

<210> 257

<211> 301

<212> DNA

<213> Homo sapien

```
<210> 258
<211> 301
<212> DNA
<213> Homo sapien
```

```
<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G
```

<400> 258						
cagcagtagt	agatgccgta	tgccagcacg	cccagcactc	ccaggatcag	caccagcacc	60
aggggcccag	ccaccaggcg	cagaagcaag	ataaacagta	ggctcaagac	cagagccacc	120
cccagggcaa	caagaatcca	ataccaggac	tggggcaaat	cttcaaagat	cttaacactg	180
atgtctcggg	cattgaggct	gtcaataana	cgctgatccc	ctgctgtatg	gtggtgtcat	240
tggtgatccc	tgggagcgcc	ggtggagtaa	cgttggtcca	tggaaagcag	cgcccacaac	300
t						301

```
<210> 259
<211> 301
<212> DNA
<213> Homo sapien
```

```
<220>  
<221> misc_feature  
<222> (1)...(301)  
<223> n = A,T,C or G
```

<400> 259						
tcatatatgc	aaacaaatgc	agactangcc	tcaggcagag	actaaaggac	atctcttggg	60
gtgtcctgaa	gtgatttgga	cccctgaggg	cagacaccta	agtaggaatc	ccagtgggaa	120
gcaaagccat	aaggaagccc	aggattcctt	gtgatcagga	agtgggccag	gaaggtctgt	180
tccagctcac	atctcatctg	catgcagcac	ggaccggatg	cgccccactg	gtcttggcct	240
ccctcccatc	ttctcaagca	gtgtccttgt	tgagccattt	gcatccttgg	ctccagggtg	300
c						301

```
<210> 260
<211> 301
<212> DNA
<213> Homo sapien
```

<b>&lt;400&gt; 260</b>						
tttttttttct	ccctaaggaa	aaagaaggaa	caagtctcat	aaaaccaa	aagcaatggt	60
aagggtgtctt	aacttgaaaa	agattaggag	tcactggttt	acaagttata	attgaatgaa	120
agaactgtaa	cagccacagt	tggccatttc	atgccaatgg	cagcaaaaaa	caggattaac	180
tagggcaaaa	taaataagtg	tgtggaagcc	ctgataagtg	cttaataaac	agactgattc	240
actgagacat	cagtacctgc	ccgggcggcc	gctcgagcgg	aattctgcag	atatccatca	300
c						301

<210> 261  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 261  
 aaatattcga gcaaattcctg taactaatgt gtctccataa aaggctttga actcagtgaa 60  
 tctgcttcca tccacgattc tagcaatgac ctctcggaca tcaaagctcc tcttaagggtt 120  
 agcaccaact attccataca attcatcagc aggaaataaa ggctcttcag aagggttcaat 180  
 ggtgacatcc aattttcttct gataatttag attcctcaca accttcctag ttaagtgaag 240  
 ggcattgatga tcatccaaag cccagtggtc acttactcca gactttctgc aatgaagatc 300  
 a 301

<210> 262  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 262  
 gaggagagcc tggttacagca tttgtaagca cagaatactc caggagtatt tgtaattgtc 60  
 tgtgagcttc ttgccgcaag tctctcagaa atttaaaaag atgcaaatcc ctgagtcacc 120  
 cctagacttc ctaaaccaga tcctctgggg ctggaacctg gcactctgca tttgtaatga 180  
 gggctttctg gtgcacacct aattttgtgc atctttgccc taaatcctgg attagtgtcc 240  
 catcattacc cccacattat aatgggatag attcagagca gatactctcc agcaaagaat 300  
 c 301

<210> 263  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 263  
 tttagcttgt ggtaaattgac tcacaaaact gattttaaaa tcaagttaat gtgaattttg 60  
 aaaattacta. cttaattccta attcacaata acaatggcat taagggttga ctgagtttg 120  
 ttcttagtat tatttatggg aaataggctc ttaccacttg caaataactg gccacatcat 180  
 taatgactga ctccccagta aggctctcta aggggtaagt angaggatcc acaggatttg 240  
 agatgctaag gccccagaga togtttgatc caacctctt attttcagag gggaaaatgg 300  
 g 301

<210> 264  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 264  
 aaagacgtta aaccactcta ctaccacttg tggaactctc aaagggtaaa tgacaaascc 60  
 aatgaatgac tctaaaaaca atatttacat ttaatgggtt gtagacaata aaaaaacaag 120  
 gtggatagat ctagaattgt aacattttta gaaaaccata scatttgaca gatgagaaag 180  
 ctcaattata gatgcaaagt tataactaaa ctactatagt agtaaagaaa tacatttcac 240  
 acccttcata taaattcact atcttggtt gaggcactcc ataaaatgta tcacgtgcat 300  
 a 301

<210> 265



<211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 265  
 tgcccaagtt atgtgtaagt gtatccgcac ccagaggtaa aactacactg tcatctttgt 60  
 cttcttgga cgcagtattt cttctctggg gagaagccgg gaagtcttct cctggctcta 120  
 catattcttg gaagtctcta atcaactttt gttccatttg tttcatttct tcaggaggga 180  
 ttttcagttt gtcaacatgt tctctaaca cacttgccca tttctgtaaa gaatccaaag 240  
 cagtccaagg ctttgacatg tcaacaacca gcataactag agtatccttc agagatacgg 300  
 c 301

<210> 266  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 266  
 taccgtctgc ctttccctcc atccaggcca tctgcgaatc tacatgggtc ctccattatcg 60  
 acaccagatc actcttttct ctaccacag gcttgctatg agcaagagac acaacctcct 120  
 ctcttctgtg ttccagcttc ttttctgtt cttccacccc ctttaagttct attcctgggg 180  
 atagagacac caatacccat aacctctctc ctaagcctcc ttataaccca ggggtgcacag 240  
 cacagactcc tgacaactgg taaggccaat gaactgggag ctcacagctg gctgtgctg 300  
 a 301

<210> 267  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 267  
 aaagagcaca ggccagctca gcctgccctg gccatctaga ctcagcctgg ctccatgggg 60  
 gttctcagtg ctgagtcctat ccaggaaaag ctcacctaga cttctgagg ctgaatcttc 120  
 atcctcacag gcagcttctg agagcctgat attcctagcc ttgatgggtc ggagtaaagc 180  
 ctcatctga ttctctctct tcttttcttt caagttggct ttctcacat ccctctgttc 240  
 aattcgcttc agcttgctg ctttagccct catttcacaga agcttcttct ctttggcctc 300  
 t 301

<210> 268  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 268  
 aatgtctcac tcaactactt ccagcctac cgtggcctaa ttctgggagt tttcttctta 60  
 gatcttggga gagctgggtc ttctaaggag aaggaggaag gacagatgta actttggatc 120  
 tcgaagagga agtctaattg aagtaattag tcaacgggtc ttgttttagac tcttggata 180  
 tgctgggtgg ctcagtgagc ctttttgag aaagcaagta ttattcttaa ggagtaacca 240  
 cttccattg ttctacttcc taccatcatc aattgtatat tatgtattct ttggagaact 300  
 a 301

<210> 269  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 269  
 taacaatata cactagctat ctttttaact gtccatcatt agcaccaatg aagattcaat 60

89

```

aaaattacct ttattcacac atctcaaaac aattctgcaa attcttagtg aagtttaact 120
atagtcacag accttaaata ttcacattgt tttctatgtc tactgaaaat aagttcacta 180
cttttctgga tattctttac aaaatcttat taaaattcct ggtattatca cccccaatta 240
tacagtagca caaccacctt atgtagtttt tacatgatag ctctgtagaa gtttcacatc 300
t 301

```

```

<210> 270
<211> 301
<212> DNA
<213> Homo sapien

```

```

<400> 270
cattgaagag cttttgcgaa acatcagaac acaagtgcct ataaaattaa ttaagcctta 60
cacaagaata catattcctt ttatttctaa ggagttaaac atagatgtag ctgatgtgga 120
gagcttgctg gtgcagtgc tttggataa cactattcat ggccgaattg atcaagtcaa 180
ccaactcctt gaactggatc atcagaagaa ggggtggtgc cgatatactg cactagataa 240
tggaaccaacc aactaaattc tctcaccagg ctgtatcagt aaactggcct aacagaaaac 300
a 301

```

```

<210> 271
<211> 301
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

```

```

<400> 271
aaaaggttct cataagatta acaattttaa taaatatttg atagaacatt ctttctcatt 60
tttatagctc atcttttaggg ttgatattca gttcatgcct cccttgctgt tottgatcca 120
gaattgcaat cacttcatca gcctgtattc gctcgaattc tctataaagt ggggtccaagg 180
tgaaccacag agccacagca cacctctttc ccttggtgac tgccttcacc ccatganggt 240
tctctcctcc agatganaac tgatcatgcy ccacattttt ggggtttata gaagcagtc 300
c 301

```

```

<210> 272
<211> 301
<212> DNA
<213> Homo sapien

```

```

<400> 272
taaattgcta agccacagat aacaccaatc aaatggaaca aatcactgtc ttcaaagtgc 60
ttatcagaaa accaaatgag cctggaatct tcataatacc taaacatgcc gtatttagga 120
tccaataatt ccctcatgat gagcaagaaa aattctttgc gcaccctcc tgcattccaca 180
gcattctctc caacaaatat aaccttgagt ggcttcttgt aatctatgtt ctttgttttc 240
ctaaggactt ccattgcatc tctacaata ttttctctac gcaccactag aattaagcag 300
g 301

```

```

<210> 273
<211> 301
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(301)

```

acatgtgtgt	atgtgtatct	ttgggaaaaan	aanaagacat	cttgtttayt	atttttttgg	60
agagangctg	ggacatggat	aatcacwtaa	tttgctayta	tyactttaat	ctgactygaa	120
gaaccgtcta	aaaataaaaat	ttaccatgtc	dtatatctct	tatagtatgc	ttatttcacc	180
ttytttctgt	ccagagagag	tatcagtgac	ananatttma	gggtgaamac	atgmattggt	240
gggacttnty	tttacngagm	accctgcccg	sgcgcctcg	makcngantt	cgcgsananc	300
						301

<213> Homo sapien

$$\langle 223 \rangle \quad n = A, T, C \text{ or } G$$

cttatatact	ctttctcaga	ggcaaaagag	gagatgggta	atgtagacaa	ttctttgagg	60
aacagtaa	gattattaga	gagaangaat	ggaccaagga	gacagaaatt	aacttgtaaa	120
tgattctctt	tggaatctga	atgagatcaa	gaggccagct	ttagcttg	gaaaagtcca	180
tctaggtatg	gttgcatctt	cgtcttcttt	tctgcagtag	ataatgaggt	aaccgaaggc	240
aattgtgctt	cttttgataa	gaagcttctt	tggtcata	aggaaattcc	aganaaagtc	300
c						301

<213> Homo sapien

<223> n = A, T, C or G

tcggtgtcag	cagcacgtgg	cattgaacat	tgcaatgtgg	agcccaaacc	acagaaaatg	60
gggtgaaatt	ggccaacttt	ctattaactt	atgttggtgcaa	ttttgccacc	aacagtaagc	120
tggcccttct	aataaaaaga	aattgaaagg	tttctcacta	aacggaatta	agtatggag	180
tcaagagact	cccaggcctc	agcgtacctg	cccggggcggc	cgctcgaagc	cgaattctgc	240
agatatccat	cacactggcg	gncgctcgan	catgcatcta	gaaggnccaa	ttcgccctat	300
a						301

<213> Homo sapien

gttacacata	ctcaataaat	aaatgactgc	atttgtggtat	tattactata	ctgattatat	60
ttatcatgtg	acttctaatt	agaaaatgta	tccaaaagca	aaacagcaga	tatacaaaat	120
taaagagaca	gaagatagac	attaacagat	aaggcaactt	atacattgag	aatccaaatc	180
caatacattt	aaacatttgg	gaaatgaggg	ggacaaatgg	aagccagatc	aaatttgtgt	240
aaaactattc	agtatgtttc	ccttgcttca	tgtctgagaa	ggctctcctt	caatggggat	300
g						301

<210> 277  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 277  
 tttgttgatg tcagtatttt attacttgcg ttatgagtgc tcacotggga aattctaaag 60  
 atacagagga cttggaggaa gcagagcaac tgaatttaat ttaaaagaag gaaaacattg 120  
 gaatcatggc actoctgata ctttcccaaa tcaacactct caatgcccc cctcgtcct 180  
 caccatagtg gggagactaa agtggccacg gatttgcctt angtgtgcag tgcgttctga 240  
 gttcnctgtc gattacatct gaccagtctc ctttttccga agtccttccg ttcaatcttg 300  
 c 301

<210> 278  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 278  
 taccactaca ctccagcctg ggcaacagag caagacctgt ctcaaagcat aaaatggaat 60  
 aacatatcaa atgaaacagg gaaaatgaag ctgacaattt atggaagcca gggcttgtca 120  
 cagtcctctac tgttattatg cattacctgg gaatttatat aagcccttaa taataatgcc 180  
 aatgaacatc tcatgtgtgc tcacaatgtt ctggcactat tataagtgtc tcacaggttt 240  
 tatgtgttct tcgttaacttt atggantagg tactcggccg cgaacacgct aagccgaatt 300  
 c 301

<210> 279  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 279  
 aaagcaggaa tgacaaagct tgcttttctg gtatgttcta ggtgtattgt gacttttact 60  
 gttatattaa ttgccaatat aagtaaatat agattatata tgtatagtgt ttcacaaagc 120  
 ttagaccttt acctccagc caccacacag tgcttgatat ttcagagtca gtcattggtt 180  
 atacatgtgt agttccaaag cacataagct agaanaanaa atatttctag ggagcactac 240  
 catctgtttt cacatgaaat gccacacaca tagaactcca acatcaattt cattgcacag 300  
 a 301

<210> 280  
 <211> 301  
 <212> DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 280

ggtactggag ttttcctccc ctgtgaaaac gtaactactg ttgggagtga attgaggatg	60
tagaaaggtg gtggaaccaa attgtggtca atggaaatag gagaatatgg ttctcactct	120
tgagaaaaaa acctaaagatt agcccaggta gttgcctgta acttcagttt ttctgcctgg	180
gtttgatata gtttaggggtt ggggttagat taagatctaa attacatcag gacaaagaga	240
cagactatta actccacagt taattaagga ggtatgttcc atgtttattt gttaaagcag	300
t	301

&lt;210&gt; 281

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 281

aggtacaaga aggggaatgg gaaagagctg ctgctgtggc attgttcaac ttggatattc	60
gccgagcaat ccaaatoctg aatgaagggg catcttctga aaaaggagat ctgaatctca	120
atgtggtagc aatggcttta tcgggttata cggatgagaa gaactccctt tggagagaaa	180
tgtgtagcac actgcgatta cagctaaata acccgatttt gtgtgtcatg ttgcatcttc	240
tgacaagtga aacaggatct tacgatggag ttttgtatga aaacaaagtt gcagtacctc	300
g	301

&lt;210&gt; 282

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 282

caggtaactac agaattaaaa tactgacaag caagtagttt cttggcgtgc acgaattgca	60
tccagaaccc aaaaattaag aaattcaaaa agacattttg tgggcacctg ctagcacaga	120
agcgagaag caaagcccag gcagaacat gctaacctta cagctcagcc tgcacagaag	180
cgcagaagca aagcccaggc agaaccatgc taaccttaca gctcagcctg cacagaagcg	240
cagaagcaaa gcccaggcag aacatgctaa cttacagct cagcctgcac agaagcacag	300
a	301

&lt;210&gt; 283

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 283

atctgtatac ggcagacaaa ctttatarag tgtagagagg tgagcgaaag gatgcaaaag	60
cactttgagg gctttataat aatatgctgc ttgaaaaaaa aaatgtgtag ttgatactca	120
gtgcatctcc agacatagta aggggttgct ctgaccaatc aggtgatcat tttttctatc	180
acttcccagg ttttatgcaa aaattttggt aaattctata atggtgatat gcattcttta	240
ggaacatat acatttttaa aaatctattt tatgtaagaa ctgacagacg aatttgcttt	300
g	301

&lt;210&gt; 284

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 284

caggtaacaaa acgctattaa gtggcttaga attgaacat ttgtggtctt tatttacttt	60
gcttcgtgtg ttggcaaagc aacatcttcc ctaaataat attaccaaga aaagcaagaa	120
gcagattagg tttttgacaa aacaaacagg ccaaaagggg gctgacctgg agcagagcat	180

ggtgagaggc aaggcatgag agggcaagtt tgttgtggac agatctgtgc ctactttatt 240  
 actggagtaa aagaaaacaa agttcattga tgtcgaagga tatatacagt gttagaaatt 300  
 a 301

<210> 285

<211> 301

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(301)

<223> n = A,T,C or G

<400> 285

acatcaccat gatcgatcc cccacccatt atacgttgta tgtttacata aatactcttc 60  
 aatgatcatt agtgttttaa aaaaaatact gaaaactcct tctgcatccc aatctctaac 120  
 caggaaagca aatgctattt acagacctgc aagccctccc tcaaacnaaa ctatttctgg 180  
 attaaatag tctgacttct tttgaggta cagcagtagg caaatgctat ttacgatctg 240  
 caaagctgt ttgaagagtc aaagccccc tgtgaacagc atttctggac cctgtaacag 300  
 t 301

<210> 286

<211> 301

<212> DNA

<213> Homo sapien

<400> 286

taccactgca ttccagcctg ggtgacagag tgagactccg tctccaaaaa aaactttgct 60  
 tgtatattat ttttgcctta cagtggatca ttctagtagg aaaggacagt aagatttttt 120  
 atcaaaatgt gtcatgccag taagagatgt tatattcttt tctcatttct tccccacca 180  
 aaaataagct accatatagc ttataagtct caaatttttg ctttttacta aaatgtgatt 240  
 gtttctgttc atttgttatg cttcatcacc tatattaggc aaattccatt ttttcccttg 300  
 t 301

<210> 287

<211> 301

<212> DNA

<213> Homo sapien

<400> 287

tacagatctg ggaactaaat attaaaaatg agtgtggctg gatatatgga gaatgttggg 60  
 ccagaagga acgtagagat cagatattac aacagctttg ttttgagggt tagaaatag 120  
 aaatgatttg gttatgaacg cacagttag gcagcagggc cagaatcctg accctctgcc 180  
 ccgtggttat ctccctccca gcttggtgc ctcagtgtat cacagtattc cattttgttt 240  
 gttgcatgtc ttgtgaagcc atcaagattt tctcgtctgt tttcctctca ttggaatgc 300  
 t 301

<210> 288

<211> 301

<212> DNA

<213> Homo sapien

<400> 288

gtacacctaa ctgcaaggac agctgaggaa tgtaatgggc agccgctttt aaagaagtag 60  
 agtcaatagg aagacaaatt ccagttccag ctcagtctgg gtatctgcaa agctgcaaaa 120  
 gatctttaa gacaatttca agagaatatt tccttaaagt tggcaatttg gagatcatc 180  
 aaaagcatct gcttttgtga tttaatttag ctcactctgg cactggaaga atccaaacag 240

tctgccttaa ttttggatga atgcatgatg gaaattcaat aatttagaaa gttaaaaaaa 300  
a 301

<210> 289  
<211> 301  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(301)  
<223> n = A,T,C or G

<400> 289  
ggtacactgt ttccatgta tgtttctaca cattgctacc tcagtgtcc tggaaactta 60  
gcttttgatg tctccaagta gtccaccttc atttaactct ttgaaactgt atcatctttg 120  
ccaagtaaga gtggtggcct atttcagctg ctttgacaaa atgactggct cctgacttaa 180  
cgttctataa atgaatgtgc tgaagcaaag tgcccatggt ggccggcgaan aagagaaaga 240  
tgtgtttgt tttggactct ctgtgtgcc ttccaatgct gtgggtttcc aaccagnnga 300  
a 301

<210> 290  
<211> 301  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(301)  
<223> n = A,T,C or G

<400> 290  
acactgagct cttcttgata aatatacaga atgcttggca tatacaagat tctatactac 60  
tgactgatct gttcatttct ctcacagctc ttaccccaa aagcttttcc accctaagtg 120  
ttctgacctc cttttotaat cacagtaggg atagaggcag anccacctac aatgaacatg 180  
gagttctatc aagaggcaga aacagcacag aatcccagtt ttaccattcg ctagcagtgc 240  
tgccttgaac aaaaacattt ctccatgtct cattttcttc atgcctcaag taacagtgag 300  
a 301

<210> 291  
<211> 301  
<212> DNA  
<213> Homo sapien

<400> 291  
caggtagcaa tttcttctat cctagaaaca ttcatcttta tgttgttgaa acataacaac 60  
tatatcagct agattttttt tctatgcttt acctgctatg gaaaatttga cacattctgc 120  
ttactcttt tgtttatagg tgaatcacia aatgtatttt tatgtattct gtagttcaat 180  
agccatggct gtttacttca tttaatttat ttagcataaa gacattatga aaaggcctaa 240  
acatgagctt cacttcccca ctaactaatt agcatctgtt atttcttaac cgtaatgcct 300  
a 301

<210> 292  
<211> 301  
<212> DNA  
<213> Homo sapien

<220>

95

<221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 292  
 accttttagt agtaatgtct aataataaat aagaaatcaa ttttataagg tccatatagc 60  
 tgtattaaat aatttttaag tttaaaagat aaaataccat catttttaaat gttggtattc 120  
 aaaaccaaag natataaccg aaaggaaaaa cagatgagac ataaaaatgat ttgcnagatg 180  
 ggaaatatag tasttyatga atgttnatta aattccagtt ataatagtgg ctacacactc 240  
 tcactacaca cacagacccc acagtccctat atgccacaaa cacatttcca taacttgaaa 300  
 a 301

<210> 293  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 293  
 ggtaccaagt gctgggtgcc gcctgttacc tgttctcact gaaaagtctg gctaattgctc 60  
 ttgtgtagtc acttctgatt ctgacaatca atcaatcaat ggcctagagc actgactggt 120  
 aacacaaaac tcaactagcaa agtagcaaca gcttttaagtc taaatacaaa gctgtttctgt 180  
 gtgagaattt tttaaaaggc tacttgtata ataacccttg tcatttttaa tgtacctcgg 240  
 ccgcgaccac gctaagccga attctgcaga tatccatcac actggcgggc gctcgagcat 300  
 g 301

<210> 294  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 294  
 tgaccataa caatatacac tagctatctt ttttaactgtc catcattagc accaatgaag 60  
 attcaataaa attaccttta ttcaacacatc tcaaaacaat totgcaaatt cttagtgaag 120  
 ttttaactata gtcacaganc ttaaattatc acattgtttt ctatgtctac tgaaaataag 180  
 ttcactactt ttctgggata ttctttacaa aatcttatta aaattcctgg tattatcacc 240  
 cccaattata cagtagcaca accaccttat gtagttttta catgatagct ctgtagaggt 300  
 t 301

<210> 295  
 <211> 305  
 <212> DNA  
 <213> Homo sapien

<400> 295  
 gtactctttc tctcccctcc tctgaattta attctttcaa cttgcaattt gcaaggatta 60  
 cacatttcac tgtgatgtat attgtgttgc aaaaaaaaaa gtgtctttgt ttaaaattac 120  
 ttggtttgtg aatccatctt gctttttccc catttggaact agtcattaac ccatctctga 180  
 actggtagaa aaacrtctga agagctagtc tatcagcatc tgacaggatga attggatggt 240  
 tctcagaacc atttcaccca gacagcctgt ttctatcctg ttttaataaat tagtttgggt 300  
 tctct 305

<210> 296  
 <211> 301



```
<212> DNA
<213> Homo sapien
```

```

<400> 296
aggctactatg ggaagctgct aaaataatat ttgatagtaa aagtatgtaa tgtgctatct      60
cacctagtag taaactaaaa ataaactgaa actttatgga atctgaagtt attttccttg      120
attaaataga attaataaac caatatgagg aaacatgaaa ccatgcaatc tactatcaac      180
tttgaaaaaag tgattgaacg aaccacttag ctttcagatg atgaacactg ataagtcatt      240
tgtcattact ataaatttta aaatctgtta ataagatggc ctatagggag gaaaaagggg      300
c                                                    301

```

```
<210> 297
<211> 300
<212> DNA
<213> Homo sapien
```

```
<220>
<221> misc_feature
<222> (1)...(300)
<223> n = A,T,C or G
```

<400> 297						
actgagtttt	aactggacgc	caagcaggca	aggctggaag	gttttgctct	ctttgtgcta	60
aaggtttttga	aaaccttgaa	ggagaatcat	tttgacaaga	agtacttaag	agtctagaga	120
acaaacangt	gaaccagctg	aaagctctcg	ggggaanctt	acatgtgttg	ttaggcctgt	180
tcocatcttg	ggagtcgact	ggccatccct	caaaatttgt	ctgggctggc	ctgagtggtc	240
accgcacctc	ggccgcgacc	acgctaagcc	gaattctgtc	gatatccatc	acactggcgg	300

```
<210> 298
<211> 301
<212> DNA
<213> Homo sapien
```

```
<220>  
<221> misc_feature  
<222> (1)...(301)  
<223> n = A,T,C or G
```

<400> 298							
tatgggggttt	gtcacccaaa	agctgatgct	gagaaaggcc	tccctggggc	ccctccgcgc		60
ggcatctgag	agacctggtg	ttccagtggt	tctggaaatg	ggtccagtg	cgcgcggctg		120
tgaagctctc	agatcaatca	cgggaagggc	ctggcgggtg	tggccacctg	gaaccaccct		180
gtcctgtctg	tttacatttc	actaycaggt	ttctctggg	cattacnatt	tgttccccta		240
caacagtgac	ctgtgcattc	tgctgtggcc	tgctgtgtct	gcaggtggct	ctcagcgagg		300
t							301

```
<210> 299
<211> 301
<212> DNA
<213> Homo sapien
```

<400> 299

gttttgagac	ggagtttcac	tcttgttgcc	cagactggac	tgcaatggca	gggtctctgc	60
tcaactgcacc	ctctgcctcc	caggttcgag	caattctcct	gcctcagcct	cccaggtagc	120
tgggattgca	ggctaacgcc	accataccca	gctaattttt	ttgtattttt	agtagagacg	180
gagtttcgcc	atgttggcca	gctggtctca	aactcctgac	ctcaagcgac	ctgcctgcct	240
cgccctccca	aagtgctgga	attataggca	tgagtcaaca	cgcccagcct	aaagatatatt	300
t						301

<210> 300  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 300  
 attcagtttt atttgctgcc ccagtatctg taaccaggag tgccacaaaa tcttgccaga 60  
 tatgtcccac acccactggg aaaggctccc acctggctac ttcctctatc agctgggtca 120  
 gctgcattcc acaaggttct cagcctaata agtttacta cctgccagtc tcaaaactta 180  
 gtaaagcaag accatgacat tccccacgg aaatcagagt ttgccccacc gtcttggtac 240  
 tataaagcct gcctctaaca gtccttgctt ottcacacca atcccgagcg catcccccat 300  
 g 301

<210> 301  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 301  
 ttaaattttt gagaggataa aaaggacaaa taatctagaa atgtgtcttc ttcagtctgc 60  
 agaggacccc aggtctccaa gcaaccacat ggtcaagggc atgaataatt aaaagttggt 120  
 gggaactcac aaagaccctc agagctgaga caccacaaac agtgggagct cacaaagacc 180  
 ctgagagctg agacacccac aacagtggga gtcacaaaag accctcagag ctgagacacc 240  
 cacaacagca cctcgttcag ctgccacatg tgtgaataag gatgcaatgt ccagaagtgt 300  
 t 301

<210> 302  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 302  
 aggtacacat ttagcttggtg gtaaataact cacaataactg attttaaaaat caagttaagt 60  
 tgaattttga aaattactac ttaattcctaa ttcacaataa caatggcatt aaggtttgac 120  
 ttgagttggt tcttagtatt atttatggta aataggctct taccacttgc aaataactgg 180  
 ccacatcatt aatgactgac ttcccagtaa ggctctctaa ggggtaagta ggaggatcca 240  
 caggatttga gatgctaagg cccagagat cgtttgatcc aaccctctta ttttcagagg 300  
 g 301

<210> 303  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 303  
 aggtaccaac tgtggaataa ggtagaggat cattttttct ttccatatca actaagttgt 60  
 atattgtttt ttgacagttt aacacatctt cttctgtcag agattctttc acaatagcac 120  
 tggctaattg aactaccgct tgcattgtaa aaatgggtgt ttgtgaaatg atcataggcc 180  
 agtaacgggt atgtttttct aactgatctt ttgctcgttc caaagggacc tcaagacttc 240  
 catcgatttt atatctgggg tctagaaaag gagttaatct gttttccctc ataaattcac 300  
 c 301

<210> 304  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 304  
 acatggatgt tatttttgag actgtcaacc tgaatttgta ttgcttgac attgcctaatt 60  
 tattagtttc agtttcagct tacccacttt ttgtctgcaa catgcaraas agacagtgcc 120  
 ctttttagtg tatcataatca ggaatcatct cacattgggt ttgtgccatta ctggtgcagt 180  
 gactttcagc cacttgggta aggtggagtt ggccatatgt ctccactgca aaattactga 240  
 ttttcctttt gtaattaata agtgtgtgtg tgaagaattct ttgagatgag gtatatatct 300  
 c 301

<210> 305  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 305  
 gangtacagc gtggtcaagg taacaagaag aaaaaaatgt gagtggcatc ctgggatgag 60  
 cagggggaca gacctggaca gacacgttgt catttgctgc tgtgggtagg aaaatgggag 120  
 taaaggagga gaaacagata caaatctcc aactcagtat taaggatttc tcatgcctag 180  
 aatattggta gaaacaagaa tacattcata tggcaaataa ctaaccatgg tggaaacaaa 240  
 ttctgggatt taagttggat accaangaaa ttgtattaaa agagctgttc atggaataag 300  
 a 301

<210> 306  
 <211> 8  
 <212> PRT  
 <213> Homo sapien

<400> 306  
 Val Leu Gly Trp Val Ala Glu Leu  
 1 5

<210> 307  
 <211> 637  
 <212> DNA  
 <213> Homo sapien

<400> 307  
 acagggatg aagggaaagg gagaggatga ggaagccccc ctggggattt ggtttgggtcc 60  
 ttgtgatcag gtggtctatg gggcttatcc ctacaaagaa gaatccagaa atagggggcac 120  
 attgaggaat gatacttgag cccaaagagc attcaatcat tgttttattt gccttmtttt 180  
 cacaccattg gtgagggagg gattaccacc ctgggggttat gaagatgggt gaacacccca 240  
 cacatagcac cggagatatg agatcaacag tttottagcc atagagattc acagcccaga 300  
 gcaggaggac gcttgcacac catgcaggat gacatggggg atgcgctcgg gattggtgtg 360  
 aagaagcaag gactgttaga ggcaggcttt atagtaacaa gacgggtggg caaactctga 420  
 tttccgtggg ggaatgtcat ggtcttgctt tactaagttt tgagactggc aggtagtga 480  
 actcattagg ctgagaacct tgtggaatgc acttgaccca sctgatatag gaagtagcca 540  
 ggtgggagcc tttcccagtg ggtgtgggac atatctggca agattttgtg gcaactcctgg 600  
 ttacagatac tggggcagca aataaaactg aatcttg 637

<210> 308  
 <211> 647  
 <212> DNA  
 <213> Homo sapien

99

<220>  
 <221> misc\_feature  
 <222> (1)...(647)  
 <223> n = A,T,C or G

<400> 308  
 acgattttca ttatcatgta aatcgggtca ctcaaggggc caaccacagc tgggagccac 60  
 tgctcagggg aaggttcata tgggactttc tactgcccaa gggtctatac aggatataaa 120  
 ggngcctcac agtatagatc tggtagcaaa gaagaagaaa caaacactga tctctttctg 180  
 ccaccctct gaccctttgg aactcctctg accctttaga acaagcctac ctaatatctg 240  
 ctagagaaaa gaccaacaac ggccctcaaag gatctcttac catgaaggtc tcagctaatt 300  
 cttgggctaag atgtgggttc cacattaggt tctgaatatg gggggaagg tcaatttgct 360  
 cattttggtg gtggataaaag tcaggatgcc caggggccag agcagggggc tgcttgcttt 420  
 gggaacaatg gctgagcata taaccatagg ttatggggaa caaaacaaca tcaaagtcac 480  
 tgtatcaatt gccatgaaga cttgaggggac ctgaatctac cgattcatct taaggcagca 540  
 ggaccagttt gagtggcaac aatgcagcag cagaatcaat ggaaacaaca gaatgattgc 600  
 aatgtccttt tttttctcct gcttctgact tgataaaagg ggaccgt 647

<210> 309  
 <211> 460  
 <212> DNA  
 <213> Homo sapien

<400> 309  
 acttttagt ttaggctgga cattggaaaa aaaaaaagc cagaacaaca tgtgatagat 60  
 aatatgattg gctgcacact tocagactga tgaatgatga acgtgatgga ctattgtatg 120  
 gagcacatct tcagcaagag ggggaaatac tcatcatttt tggccagcag ttgtttgatc 180  
 accaaacatc atgccagaat actcagcaaa ccttcttagc tottgagaag tcaaagtcag 240  
 ggggaattta ttcttgcaa ttttaattgg actccttatg tgagagcagc ggctaccag 300  
 ctgggggtgt ggagcgaacc cgtcactagt ggacatgcag tggcagagct cctggtaacc 360  
 acctagagga atacacaggc acatgtgtga tgccaagcgt gacacctgta gcactcaaat 420  
 ttgtcttgtt tttgtctttc ggtgtgtaag attcttaagt 460

<210> 310  
 <211> 539  
 <212> DNA  
 <213> Homo sapien

<400> 310  
 acgggactta tcaataaag ataggaaaag aagaaaactc aaatattata ggcagaaatg 60  
 ctaaagggtt taaaatatgt caggattgga agaaggcatg gataaagaac aaagttcagt 120  
 taggaaagag aaacacagaa ggaagagaca caataaaagt cattatgtat tctgtgagaa 180  
 gtcagacagt aagatttgtg ggaaatgggt tgggtttgtg tatgggtatg attttagcaa 240  
 taatctttat ggcagagaaa gctaaaatcc tttagcttgc gtgaatgatc acttgctgaa 300  
 ttctcaagg taggcatgat gaaggagggt ttagaggaga cacagacaca atgaactgac 360  
 ctagatagaa agccttagta tactcagcta ggaatagtga ttctgagggc acactgtgac 420  
 atgattatgt cattacatgt atggtagtga tggggatgat aggaaggaag aacttatggc 480  
 atattttcac cccacaaaa gtcagttaaa tattgggaca ctaaccatcc aggtcaaga 539

<210> 311  
 <211> 526  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(526)  
 <223> n = A,T,C or G

100

```

<400> 311
caaatttgag ccaatgacat agaattttac aaatcaagaa gcttattctg gggccatttc      60
ttttgacgtt ttotctaaac tactaaagag gcattaatga tccataaatt atattatcta      120
catttacagc atttaaaatg tgttcagcat gaaatattag ctacagggga agctaaataa      180
attaaacatg gaataaagat ttgtccttaa atataatcta caagaagact ttgatatttg      240
tttttcacaa gtgaagcatt cttataaagt gtcataacct ttttggggaa actatgggaa      300
aaaatgggga aactctgaag ggttttaagt atcttacctg aagctacaga ctccataacc      360
tctctttaca gggagctcct gcagccccta cagaaatgag tggctgagat tcttgattgc      420
acagcaagag cttctcatct aaaccctttc cttttttagt atctgtgtat caagtataaa      480
agttctataa actgtagtnt acttatttta atccccaaag cacagt                    526

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```

<210> 312
<211> 500
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(500)
<223> n = A,T,C or G

```

```

<400> 312
cctctctctc cccaccccct gactctagag aactgggttt tctcccagta ctccagcaat      60
tcattttctga aagcagttga gccactttat tccaaagtac actgcagatg ttcaaactct      120
ccattttctct ttoccttcca cctgccagtt ttgctgactc tcaacttgtc atgagtgtaa      180
gcattaagga cattatgctt cttcgattct gaagacaggc cctgctcatg gatgactctg      240
gcttcttagg aaaatatttt tcttccaaaa tcagtaggaa atctaaactt atcccctctt      300
tgcagatgtc tagcagcttc agacatttgg ttaagaaccc atgggaaaaa aaaaaatcct      360
tgctaattgt gtttcctttg taaaccanga ttcttatttg nctgggtatag aatatcagct      420
ctgaacgtgt ggtaaagatt tttgtgtttg aatataggag aaatcagttt gctgaaaagt      480
tagtcttaat tatctatttg

```

```

<210> 313
<211> 718
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(718)
<223> n = A,T,C or G

```

```

<400> 313
ggagatttgt gtggtttgca gccgagggag accaggaaga tctgcatggt gggaaggacc      60
tgatgataca gaggtgagaa ataagaaagg ctgctgactt taccatctga ggccacacat      120
ctgctgaaat ggagataatt aacatcacta gaaacagcaa gatgacaata taatgtctaa      180
gtagtacat gtttttgcac atttcagcc cttttaata tccacacaca caggaagcac      240
aaaaggaagc acagagatcc ctgggagaaa tgcccgccg ccatottggg tcatcgatga      300
gcctcgccct gtgcctgntc ccgcttgatg gggaaggaca ttagaaaatg aattgatgtg      360
ttccttaaag gatggcagga aaacagatcc tgttggtgat atttatttga acgggattac      420
agatttgaaa tgaagtcaca aagtgcagat taccaatgag aggaaaaacag acgagaaaat      480
cttgatggtt cacaagacat gcaacaaaca aaatggaata ctgtgatgac acgagcagcc      540
aactggggag gagataccac ggggcagagg tcaggattct ggccctgctg cctaactgtg      600
cgttatacca atcatttcta tttctaccct caaacaagct gtngaataac tgacttacgg      660
ttctnttggc ccacattttc atnatccacc ccntcntttt aannttantc caaantgt      718

```

```

<210> 314

```

<211> 358  
 <212> DNA  
 <213> Homo sapien

<400> 314  
 gtttattttac attacagaaa aaacatcaag acaatgtata ctatttcaaa tataatccata 60  
 cataatcaaa tatagctgta gtacatgttt tcattgggtg agattaccac aaatgcaagg 120  
 caacatgtgt agatctcttg tcttattctt ttgtctataa tactgtattg tgtagtccaa 180  
 gctctcggtg gtccagccac tgtgaaacat gctcccttta gattaacctc gtggacgctc 240  
 ttgttgtatt gctgaactgt agtgccctgt attttgcctc tgtctgtgaa ttctgttgot 300  
 tctggggcat ttccttgtga tgcagaggac caccacacag atgacagcaa tctgaatt 358

<210> 315  
 <211> 341  
 <212> DNA  
 <213> Homo sapien

<400> 315  
 taccacctcc ccgctggcac tgatgagccg catcaccatg gtcaccagca ccatgaaggc 60  
 ataggatgat atgaggacat ggaatgggccc cccaaggatg gtctgtccaa agaagcgagt 120  
 gacccccatt ctgaagatgt ctggaacctc taccagcagg atgatgatag ccccaatgac 180  
 agtcaccagc tccccgacca gccggatata gtccttaggg gtcattgtagg ctccctgaag 240  
 tagcttctgc tgtaagaggg tgttgtcccg ggggctcgtg cggttatttg tcctgggctt 300  
 gagggggcgg tagatgcagc acatgggtgaa gcagatgatg t 341

<210> 316  
 <211> 151  
 <212> DNA  
 <213> Homo sapien

<400> 316  
 agactgggca agactcttac gccccacact gcaatttggg ctgtgtgccg tatccattta 60  
 tgtgggcctt tctcgagttt ctgattataa acaccactgg agcgatgtgt tgactggact 120  
 cattcaggga gctctggttg caatattagt t 151

<210> 317  
 <211> 151  
 <212> DNA  
 <213> Homo sapien

<400> 317  
 agaactagtg gatcctaata aaataacctga aacatatatt ggcattttatc aatgggtcaa 60  
 atctttcattt atctctggcc ttaaccttgg ctccctgaggc tgcggccagc agatcccagg 120  
 ccagggtctt gttcttgcca cacctgcttg a 151

<210> 318  
 <211> 151  
 <212> DNA  
 <213> Homo sapien

<400> 318  
 actggtggga ggcgctgttt agttggctgt ttccagaggg gtctttcgga gggacctcct 60  
 gctgcaggct ggagtgtctt tattcctggc gggagaccgc acattccact gctgaggctg 120  
 tgggggcggg ttatcaggca gtgataaaca t 151

<210> 319  
 <211> 151  
 <212> DNA

102

&lt;213&gt; Homo sapien

&lt;400&gt; 319

aactagtggga tccagagcta taggtacagt gtgatctcag ctttgcaaac acattttcta	60
catagatagt actaggtatt aatagatatg taaagaaaga aatcacacca ttaataatgg	120
taagattggg tttatgtgat tttagtgggt a	151

&lt;210&gt; 320

&lt;211&gt; 150

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 320

aactagtggga tccactagtc cagtgtggtg gaattccatt gtgttggggt tctagatcgc	60
gagcggctgc cctttttttt tttttttttg ggggggaatt tttttttttt aatagttatt	120
gagtgttcta cagcttacag taaataccat	150

&lt;210&gt; 321

&lt;211&gt; 151

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 321

agcaactttg tttttcatcc aggttatattt aggcttagga tttcctctca cactgcagtt	60
taggggtggca ttgtaaccag ctatggcata ggtgttaacc aaaggctgag taaacatggg	120
tgctctgag aaatcaaagt cttcatacac t	151

&lt;210&gt; 322

&lt;211&gt; 151

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(151)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 322

atccagcatc ttctcctggt tcttgccctc ctttttcttc ttcttasatt ctgcttgagg	60
tttgggcttg gtcagtttgc cacagggctt ggagatggtg acagtcttct ggcattcggc	120
attgtgcagg gctcgttca nacttccagt t	151

&lt;210&gt; 323

&lt;211&gt; 151

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(151)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 323

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&lt;210&gt; 324

103

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 <223> n = A,T,C or G

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 <212> DNA  
 <213> Homo sapien

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 <211> 1215  
 <212> DNA  
 <213> Homo sapien

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104

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 <211> 220  
 <212> PRT  
 <213> Homo sapien

<400> 327  
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 Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu Gly  
 35 40 45  
 Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val Glu  
 50 55 60  
 Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu Leu Ala  
 65 70 75 80  
 Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser Asp  
 85 90 95  
 Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly Asn  
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 Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg Met Pro  
 115 120 125  
 Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu Val Cys  
 130 135 140  
 Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys Ala Gly  
 145 150 155 160  
 Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly Gly Pro  
 165 170 175  
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 <212> DNA  
 <213> Homo sapien

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 atccgcagtg ggtgctgtca gccacacact gtttcagaaa ctctacacc atcgggctgg 180  
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<210> 329  
 <211> 77  
 <212> PRT  
 <213> Homo sapien

<400> 329  
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105

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		35					40					45			
His	Cys	Phe	Gln	Asn	Ser	Tyr	Thr	Ile	Gly	Leu	Gly	Leu	His	Ser	Leu
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<210> 330
<211> 70
<212> DNA
<213> Homo sapien
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<210> 331
<211> 22
<212> PRT
<213> Homo sapien
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<210> 332
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 <212> DNA  
 <213> Homo sapien

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&lt;210&gt; 334

&lt;211&gt; 2417

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 334

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&lt;211&gt; 2984

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 335

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<210> 336
<211> 147
<212> PRT
<213> Homo sapien

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20          25          30
Pro Lys Gln Pro Gln Lys Arg Ser Arg Ala Ala Phe Ser His Thr Gln
35          40          45
Val Ile Glu Leu Glu Arg Lys Phe Ser His Gln Lys Tyr Leu Ser Ala
50          55          60
Pro Glu Arg Ala His Leu Ala Lys Asn Leu Lys Leu Thr Glu Thr Gln
65          70          75          80
Val Lys Ile Trp Phe Gln Asn Arg Arg Tyr Lys Thr Lys Arg Lys Gln
85          90          95
Leu Ser Ser Glu Leu Gly Asp Leu Glu Lys His Ser Ser Leu Pro Ala
100          105          110
Leu Lys Glu Glu Ala Phe Ser Arg Ala Ser Leu Val Ser Val Tyr Asn
115          120          125
Ser Tyr Pro Tyr Tyr Pro Tyr Leu Tyr Cys Val Gly Ser Trp Ser Pro
130          135          140
Ala Phe Trp
145

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<210> 337
<211> 9
<212> PRT
<213> Homo sapien

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<400> 337
Ala Leu Thr Gly Phe Thr Phe Ser Ala
1          5

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<210> 338
<211> 9
<212> PRT
<213> Homo sapien

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<400> 338
Leu Leu Ala Asn Asp Leu Met Leu Ile
1          5

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<210> 339
<211> 318
<212> PRT
<213> Homo sapien

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110

<400> 339  
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 Cys Thr Ser Thr Val Gln Leu Pro Gly Lys Val Val Val Val Thr Gly  
 35 40 45  
 Ala Asn Thr Gly Ile Gly Lys Glu Thr Ala Lys Glu Leu Ala Gln Arg  
 50 55 60  
 Gly Ala Arg Val Tyr Leu Ala Cys Arg Asp Val Glu Lys Gly Glu Leu  
 65 70 75 80  
 Val Ala Lys Glu Ile Gln Thr Thr Thr Gly Asn Gln Gln Val Leu Val  
 85 90 95  
 Arg Lys Leu Asp Leu Ser Asp Thr Lys Ser Ile Arg Ala Phe Ala Lys  
 100 105 110  
 Gly Phe Leu Ala Glu Glu Lys His Leu His Val Leu Ile Asn Asn Ala  
 115 120 125  
 Gly Val Met Met Cys Pro Tyr Ser Lys Thr Ala Asp Gly Phe Glu Met  
 130 135 140  
 His Ile Gly Val Asn His Leu Gly His Phe Leu Leu Thr His Leu Leu  
 145 150 155 160  
 Leu Glu Lys Leu Lys Glu Ser Ala Pro Ser Arg Ile Val Asn Val Ser  
 165 170 175  
 Ser Leu Ala His His Leu Gly Arg Ile His Phe His Asn Leu Gln Gly  
 180 185 190  
 Glu Lys Phe Tyr Asn Ala Gly Leu Ala Tyr Cys His Ser Lys Leu Ala  
 195 200 205  
 Asn Ile Leu Phe Thr Gln Glu Leu Ala Arg Arg Leu Lys Gly Ser Gly  
 210 215 220  
 Val Thr Thr Tyr Ser Val His Pro Gly Thr Val Gln Ser Glu Leu Val  
 225 230 235 240  
 Arg His Ser Ser Phe Met Arg Trp Met Trp Trp Leu Phe Ser Phe Phe  
 245 250 255  
 Ile Lys Thr Pro Gln Gln Gly Ala Gln Thr Ser Leu His Cys Ala Leu  
 260 265 270  
 Thr Glu Gly Leu Glu Ile Leu Ser Gly Asn His Phe Ser Asp Cys His  
 275 280 285  
 Val Ala Trp Val Ser Ala Gln Ala Arg Asn Glu Thr Ile Ala Arg Arg  
 290 295 300  
 Leu Trp Asp Val Ser Cys Asp Leu Leu Gly Leu Pro Ile Asp  
 305 310 315

<210> 340  
 <211> 483  
 <212> DNA  
 <213> Homo sapien

<400> 340  
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 ctctgtctgc aggtctggagt gtctttattc ctggcgggag accgcacatt ccaactgctga 180  
 gggttggtggg gcggtttatc aggcagtgat aaacataaga tgtcatttcc ttgactccgg 240  
 ccttcaattt tctctttggc tgacgacgga gtccgtggtg tcccgatgta actgaccct 300  
 gctccaaacg tgacatcact gatgctcttc tctgggggtgc tgatggcccg cttgggtcacg 360  
 tgetcaatct cgccattcga ctcttgctcc aaactgtatg aagacacctg actgcacggt 420  
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 ctg 483

111

<210> 341  
 <211> 344  
 <212> DNA  
 <213> Homo sapien

<400> 341  
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 gctgccttac aagtattataa tatttttactt ctttocataa agagtagctc aaaatatgca 180  
 attaatttaa taattttctga tgatgggttt atctgcagta atatgtatat catctattag 240  
 aattttactta atgaaaaact gaagagaaca aaatttgtaa ccactagcac ttaagtactc 300  
 ctgattctta acattgtctt taatgaccac aagacaacca acag 344

<210> 342  
 <211> 592  
 <212> DNA  
 <213> Homo sapien

<400> 342  
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 caatgtggaa acttcttata cttgggttcca ttatgaagtt ggacaattgc tgctatcaca 120  
 cctggcaggt aaaccaatgc caagagagtg atggaaacca ttggcaagac tttgttgatg 180  
 accaggattg gaattttata aaaatattgt tgatgggaag ttgctaaagg gtgaattact 240  
 tccctcagaa gagtgtaaag aaaagtcaga gatgctataa tagcagctat tttaattggc 300  
 aagtgccact gtggaaagag ttccctgtgtg tgctgaagtt ctgaagggca gtcaaattca 360  
 tcagcatggg ctgtttggtg caaatgcaaa agcacaggtc tttttagcat gctggctctc 420  
 ccggtgtcct tatgcaaata atcgtcttct tctaaatttc tcctaggctt cattttccaa 480  
 agttcttctt ggtttgtgat gtcttttctg ctttccatta attctataaa atagtatggc 540  
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<210> 343  
 <211> 382  
 <212> DNA  
 <213> Homo sapien

<400> 343  
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 ctgactgccc aaggggctca gaacccagc aatcccttcc tttcactacc ttcttttttg 300  
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 aaaccaccaa gctgaaaaaa aa 382

<210> 344  
 <211> 536  
 <212> DNA  
 <213> Homo sapien

<400> 344  
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 gtttaggggg atgccaaagg taaggccagc tcagttatat gaagagaagc agaacaaaca 180  
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 ccttcttatt atttgatcta gaaattgccc tccttttacc cctaccatga gccctacaaa 420



112

caactaacct gccactaata gttatgtcat ccctcttatt aatcatcatc ctagccctaa 480  
gtctggccta tgagtgacta caaaaaggat tagactgagc cgaataacaa aaaaaa 536

<210> 345  
<211> 251  
<212> DNA  
<213> Homo sapien

<400> 345  
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gcgtgggcca ggaaatcaca tcctacactg cccaggagcc agacacattt atggaacaga 180  
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gtgccatttc c 251

<210> 346  
<211> 282  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(282)  
<223> n = A,T,C or G

<400> 346  
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ctaagtcttg ttaccaaaaa aaggaaaaag aaaagatctt ctgagttaca aattctggga 120  
aggagacta tacctggctc ttgccctaag tgagaggtct tccctccgc accaaaaat 180  
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ggtctcatth cccaaggtgc cttcaatgct catnaaaacc aa 282

<210> 347  
<211> 201  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(201)  
<223> n = A,T,C or G

<400> 347  
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tctgagactg actggaccca cccagaccca gggcaaagat acatgttacc atatcatctt 180  
tataaagaat ttttttttgt c 201

<210> 348  
<211> 251  
<212> DNA  
<213> Homo sapien

<400> 348  
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aggagacact cccagcatgg aggagggttt atcttttcat cctaggtcag gtctacaatg 180  
ggggaagggt ttattataga actcccaaca gccacctca ctctgccac ccaccgatg 240

113

gccctgcctc c 251

&lt;210&gt; 349

&lt;211&gt; 251

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 349

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cagaagggtc tgaactctac gtgttaccag agaacataat gcaattcatg cattccactt	180
agcaattttg taaaatacca gaaacagacc ccaagagtct ttcaagatga ggaaaattca	240
actcctggtt t	251

&lt;210&gt; 350

&lt;211&gt; 908

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 350

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aatgcgag	908

&lt;210&gt; 351

&lt;211&gt; 472

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 351

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gtcaaacctt aatgccattg ttattgtgaa ttaggattaa gtagtaattt tcaaaattca	120
cattaacttg attttaaaat cagwtttgyg agtcatttac cacaagctaa atgtgtacac	180
tatgataaaa acaaccattg tattcctggt tttctaaaca gtccctaattt ctaacactgt	240
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gatctgtcca caacaaactt gccctctcat gccttgccctc tcaccatgct ctgctccagg	360
tcagccccct tttggcctgt ttgttttgtc aaaaacctaa tctgcttctt gcttttcttg	420
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&lt;210&gt; 352

&lt;211&gt; 251

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 352

114

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tgtggataag	gccaggtcaa	tggctgcaag	catgcagaga	aagaggtaca	tccgagcgtg	120
caggctgcgt	tccgtcctta	cgatgaagac	cacgatgcag	tttccaaaca	ttgccactac	180
atacatggaa	aggaggggga	agccaaccca	gaaatgggct	ttctctaate	ctgggatacc	240
aataagcaca	a					251

<210> 353  
 <211> 436  
 <212> DNA  
 <213> Homo sapien

<400> 353						
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cacattatgg	tattattact	atactgatta	tatttatcat	gtgacttcta	attaraaaat	120
gtatccaaaa	gcaaaacagc	agatatacaa	aattaaagag	acagaagata	gacattaaca	180
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gggtccttaa	tgtagt					436

<210> 354  
 <211> 854  
 <212> DNA  
 <213> Homo sapien

<400> 354						
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acacgggatg	tcag					854

<210> 355  
 <211> 676  
 <212> DNA  
 <213> Homo sapien

<400> 355						
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atccacaagt	catacctgga	tgtcagcgaa	gagggcacgg	aggcagcagc	agccactggg	180
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tcatctgcaa	aataaggctca	ggatttcttc	caaccatttc	atgagttgtg	aagctaaggc	480
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115

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ggtgtctcat ttgagtgtc tccagtgtc tgatcaagtc aatgagtaaa attttaaggg 600
attagatttt cttgacttgt atgtatctgt gagatcttga ataagtgtacc tgacatctct 660
gcttaaagaa aaccag 676

```

```

<210> 356
<211> 574
<212> DNA
<213> Homo sapien

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<400> 356
tttttttttt ttttttcagga aaacattctc ttactttatt tgcattctcag caaagggttct 60
catgtggcac ctgactggca tcaaaccaaa gttcgttaggc caacaaagat gggccactca 120
caagcttccc atttgtagat ctcagtgcct atgagtatct gacacctgtt cctctcttca 180
gtctcttagg gaggttataa tctgtctcag gtgtgctaag agtgccagcc caaggkggtc 240
aaaagtccac aaaactgcag tctttgtctg gatagtaagc caagcagtgc ctggacagca 300
gagttctttt cttgggcaac agataaccag acaggactct aatcgtgtct ttattcaaca 360
ttcttctgtc tctgcctaga ctggaataaa aagccaatct ctctcgtggc acaggggaagg 420
agatacaagc tcgtttacat gtgatagatc taacaaaggc atctaccgaa gtctgggtctg 480
gatagacggc acagggagct cttaggtcag cgctgctggt tggaggacat tctgtagtcc 540
agcttttgag cctttgtgca acagtacttt ccca 574

```

```

<210> 357
<211> 393
<212> DNA
<213> Homo sapien

```

```

<400> 357
tttttttttt tttttttttt tttttttttt tacagaatat aratgcttta tcaactgkact 60
taatatggkg kcttyttcac tatacttaaa aatgcaccac tcataaatat ttaattcagc 120
aagccacaac caaracttga ttttatcaac aaaaaccctt aaatataaac ggsaaaaaag 180
atagatatata ttattccagt ttttttaaaa cttaaaarat attccattgc cgaattaara 240
araarataag tgttatatgg aaagaagggc attcaagcac actaaaraaa cctgaggkaa 300
gcataatctg tacaaaatta aactgtcctt tttggcattt taacaaattt gcaacgktct 360
tttttttctt tttctgtttt tttttttttt tac 393

```

```

<210> 358
<211> 630
<212> DNA
<213> Homo sapien

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```

<400> 358
acagggtaaa caggaggatc cttgctctca cggagcttac attctagcag gaggacaata 60
ttaatgttta taggaaaatg atgagtttat gacaaaggaa gtagatagtg ttttacaaga 120
gcatagagta gggaagctaa tccagcacag ggaggtcaca gagacatccc taaggaagtg 180
gagtttaaac tgagagaagc aagtgcctaa actgaaggat gtgttgaaaga agaagggaga 240
gtagaacaat ttgggcagag ggaaccttat agaccctaag gtgggaaggt tcaaagaact 300
gaaagagagc tagaacagct ggagccgttc tccggtgtaa agaggagtca aagagataag 360
attaagatg tgaagattaa gatcttggtg gcattcaggg attggcactt ctacaagaaa 420
tcaactgaag gagtaatgtg acattacttt tcaactcagg atggccattc taactccagg 480
gggtagactg gactaggtaa gactggaggc aggttagacct cttctaaggc ctgcgatagt 540
gaaagacaaa aataagtggg gaaattcagg ggatagttaa aatcagtagg acttaatgag 600
caagccagag gttcctccac aacaaccagt 630

```

```

<210> 359
<211> 620
<212> DNA
<213> Homo sapien

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116

&lt;400&gt; 359

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taattaaaaa	atgctactaa	tatagaaaat	ttataatcag	aaaaataaat	attcagggag	120
ctcaccagaa	gaataaagt	ctctgccagt	tattaaagga	ttactgctgg	tgaattaaat	180
atggcattcc	ccaagggaaa	tagagagatt	cttctggatt	atgttcaata	tttatttcac	240
aggattaact	gttttaggaa	cagatataaa	gcttcgccac	ggaagagatg	gacaaagcac	300
aaagacaaca	tgatacctta	ggaagcaaca	ctacccttcc	aggcataaaa	tttgagaaaa	360
tgcaacatta	tgcttcatga	ataatatgta	gaaagaaggt	ctgatgaaaa	tgacatcctt	420
aatgtaagat	aactttataa	gaattctggg	tcaaataaaa	ttctttgaag	aaaacatcca	480
aatgtcattg	acttatcaaa	tactatcttg	gcataatacc	tatgaaggca	aaactaaaca	540
aacaaaaagc	tcacacccaa	caaaaccatc	aacttatttt	gtattctata	acatacgaga	600
ctgtaaagat	gtgacagtgt					620

&lt;210&gt; 360

&lt;211&gt; 431

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 360

aaaaaaaaaa	agccagaaca	acatgtgata	gataatatga	ttggctgcac	acttcagac	60
tgatgaatga	tgaacgtgat	ggactattgt	atggagcaca	tcttcagcaa	gagggggaaa	120
tactcatcat	ttttggccag	cagttgtttg	atcaccaaac	atcatgccag	aatactcagc	180
aaaccttctt	agctcttgag	aagtcaaagt	ccgggggaat	ttattcctgg	caattttaat	240
tggaactcctt	atgtgagagc	agcggctacc	cagctggggt	ggtggagcga	acccgtcact	300
agtggaacatg	cagtggcaga	gctcctggta	accacctaga	ggaatacaca	ggcacatgtg	360
tgatgccaag	cgtgacacct	gtagcactca	aatttgtctt	gtttttgtct	ttcgggtgtgt	420
agattcttag	t					431

&lt;210&gt; 361

&lt;211&gt; 351

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 361

acactgattt	ccgatcaaaa	gaatcatcat	ctttaccttg	acttttcagg	gaattactga	60
actttcttct	cagaagatag	ggcacagcca	ttgccttggc	ctcacttgaa	gggtctgcat	120
ttgggtctct	tggtctcttg	ccaagtctcc	cagccactcg	agggagaaat	atcgggaggt	180
ttgacttcct	ccggggcttt	cccaggggct	tcaccgtgag	ccctgcggcc	ctcagggctg	240
caatcctgga	ttcaatgtct	gaaacctcgc	tctctgcctg	ctggacttct	gaggccgtca	300
ctgccactct	gtcctccagc	tctgacagct	cctcatctgt	ggtcctgttg	t	351

&lt;210&gt; 362

&lt;211&gt; 463

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 362

acttcatcag	gccataatgg	gtgcctcccg	tgagaatcca	agcacctttg	gactgcgcga	60
tgtagatgag	ccggtgaag	atcttgccga	tgccgggctt	cagggcgaag	ttcttggcgc	120
ccccggtcac	agaaatgacc	aggttgggtg	ttttcagggt	ccagtgcctg	gtcagcagct	180
cgtaaaggat	ttccgcgtcc	gtgtcgcagg	acagacgtat	atacttccct	ttcttcccca	240
gtgtctcaaa	ctgaatatcc	ccaaaggcgt	cggtaggaaa	ttccttgggt	tgtttcttgt	300
agttccattt	ctcacttttg	ttgatctggg	tgcttccat	gtgctggctc	tgggcatagc	360
cacacttgca	cacattctcc	ctgataagca	cgatgggtgt	gacaggaagg	aaggatttca	420
ttgagcctgc	ttatggaaac	tggtattgtt	agcttaata	gac		463

&lt;210&gt; 363

&lt;211&gt; 653

117

<212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(653)  
 <223> n = A,T,C or G

<400> 363  
 acccccaggt ncctgnctgg catactgnga acgaccaacg acacacccaa gctcggcctc 60  
 ctcttgngga ttctgggtga catcttcatg aatggcaacc gtgccagwga ggctgtcctc 120  
 tgggaggcac tacgcaagat gggactgctg cctgggggtga gacatcctct ccttgagatg 180  
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 ccaacagcaa cccccggaa gtatgagttc ctctrgggcc tccgttccta ccatgagasc 300  
 tagcaagatg naagtgttga gantcattgc agagggttcag aaaagagacc cntcgtgact 360  
 ggtctgcaca gtccatggag gctgcagatg aggccttgga tgctctggat gctgctgcag 420  
 ctgaggccga agcccgggt gaagcaagaa cccgcctggg aattggagat gaggctgtgt 480  
 ntgggccctg gagctgggat gacattgagt ttgagctgct gacctgggat gaggaaggag 540  
 attttgaga tccntggtcc agaattccat ttaccttctg ggccagatac caccagaatg 600  
 cccgtccag attccctcag acctttgccg gtoccattat tggctcstggt ggt 653

<210> 364  
 <211> 401  
 <212> DNA  
 <213> Homo sapien

<400> 364  
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 acaaagccaa tgaatgactc taaaaacaat atttacattt aatgggtttgt agacaataaa 120  
 aaaacaaggt ggatagatct agaattgtaa cattttaaga aaaccatagc atttgacaga 180  
 tgagaaagct caattataga tgcaaagtta taactaaact actatagtag taaagaaata 240  
 catttcacac ccttcataata aattcactat cttggcttga ggcactccat aaaatgtatc 300  
 acgtgcatag taaatcttta tatttgctat ggcgttgac tagaggactt ggactgcaac 360  
 aagtggatgc gcggaaaatg aaatcttctt caatagccca g 401

<210> 365  
 <211> 356  
 <212> DNA  
 <213> Homo sapien

<400> 365  
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 atgtttcagt gctagagcgt aggaatagac cctggcgctc actgtgagat gttcttcagc 120  
 taccagagca tcaagtctct gcagcaggtc attcttgggt aaagaaatga cttccacaaa 180  
 ctctccatcc cctggctttg gcttcggcct tgcggttttcg gcatcatctc cgtaaatggt 240  
 gactgtcacg atgtgtatag tacagtttga caagcctggg tccatacaga ccgctggaga 300  
 acattcggca atgtcccctt tgtagccagt ttcttcttcg agctcccga gagcag 356

<210> 366  
 <211> 1851  
 <212> DNA  
 <213> Homo sapien

<400> 366  
 tcataccat tgccagcagc ggcaccgtta gtcaggtttt ctgggaatcc cacatgagta 60  
 cttccgtgtt cttcattctt cttcaatagc cataaatctt ctagctctgg ctggctgttt 120  
 tcaacttcct taagcctttg tgactcttcc totgatgtca gctttaagtc ttgttctgga 180  
 ttgctgtttt cagaagagat ttttaacatc tgtttttctt tgtagtcaga aagtaactgg 240

caaattacat	gatgatgact	agaaacagca	tactctctgg	ccgtctttcc	agatcttgag	300
aagatacatc	aacattttgc	tcaagtagag	ggctgactat	acttgctgat	ccacaacata	360
cagcaagtat	gagagcagtt	cttccatata	tatccagcgc	atttaaattc	gcttttttct	420
tgattaaaa	tttcaccact	tgctgttttt	gctcatgtat	accaagtagc	agtgggtgta	480
ggccatgctt	gttttttgat	tcgatatacag	caccgtataa	gagcagtgct	ttggccatta	540
atttatcttc	attgtagaca	gcatagtgta	gagtggtatt	tccatactca	tctggaatat	600
ttggatcagt	gccatgttcc	agcaacatta	acgcacattc	atcttcctgg	cattgtacgg	660
cctttgtcag	agctgtcctc	ttttgtttgt	caaggacatt	aagttgacat	cgtctgtcca	720
gcacgagttt	tactacttct	gaattcccat	tggcagaggc	cagatgtaga	gcagtcctct	780
tttgcttgtc	cctcttggtc	acatccgtgt	ccctgagcat	gacgatgaga	tcctttctgg	840
ggactttacc	ccaccaggca	gctctgtgga	gcttgtccag	atcttctcca	tggacgtggt	900
acctgggac	ctgaaggcg	ctgtcatcgt	agtctcccca	agcgaccacg	ttgctcttgc	960
cgtctccctg	cagcagggga	agcagtgcca	gcaccacttg	cacctcttgc	tccaagcgt	1020
cttcacagag	gagtcgttgt	ggtctccaga	agtgccacg	ttgctcttgc	cgtctccct	1080
gtccatccag	ggaggaagaa	atgcaggaaa	tgaagatgc	atgcacgatg	gtatactcct	1140
cagccatcaa	acttctggac	agcaggtcac	ttccagcaag	gtggagaaag	ctgtccaccc	1200
acagaggatg	agatccagaa	accacaatat	ccattcacaa	acaaacactt	ttcagccaga	1260
cacaggtact	gaaatcatgt	catctgcggc	aacatggtgg	aacctaccca	atcacacatc	1320
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aatataattt	tcctctggag	ccatatggat	gaactatgaa	ggaagaactc	cccgaagaag	1440
ccagtcgcag	agaagccaca	ctgaagctct	gtcctcagcc	atcagcgcca	cggacaggar	1500
tggttttctt	ccccagtgat	gcagcctcaa	gttatcccga	agctgccgca	gcacacggtg	1560
gctcctgaga	aacaccccag	ctcttccggt	ctaacacagg	caagtcaata	aatgtgataa	1620
tcacataaac	agaattaaaa	gcaaagtcac	ataagcatct	caacagacac	agaaaaggca	1680
tttgacaaaa	tccagcatcc	ttgtatttat	tggtgcagtt	ctcagaggaa	atgcttctaa	1740
cttttcccca	tttagtatta	tggtggtgtg	gggcttgcta	taggtgggtt	ttattacttt	1800
aaggtagtgc	ccttctatgc	ctgttttgct	gagggtttta	attctcgtgc	c	1851

<210> 367  
 <211> 668  
 <212> DNA  
 <213> Homo sapien

<400> 367						
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acctataag	agcagtgctt	tggccattaa	tttatctttc	attrtagaca	gcrtagtgya	180
gagtggtatt	tccataactca	tctggaatat	ttggatcagt	gccatgttcc	agcaacatta	240
acgcacattc	atcttcctgg	cattgtacgg	cctgtcagta	ttagacccaa	aaacaaatta	300
catatcttag	gaattcaaaa	taacattcca	cagctttcac	caactagtta	tatttaaagg	360
agaaaactca	tttttatgcc	atgtattgaa	atcaaaacca	cctcatgctg	atatagttgg	420
ctactgcata	cctttatcag	agctgtcctc	ttttgtttgt	caaggacatt	aagttgacat	480
cgtctgtcca	gcaggagttt	tactacttct	gaattcccat	tggcagaggc	cagatgtaga	540
gcagtcctat	gagagtgaga	agacttttta	ggaaattgta	gtgcactagc	tacagccata	600
gcaatgattc	atgtaactgc	aaacactgaa	tagcctgcta	ttactctgcc	ttcaaaaaaa	660
aaaaaaa						668

<210> 368  
 <211> 1512  
 <212> DNA  
 <213> Homo sapien

<400> 368						
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gaagtagtaa	aactcstgct	ggacagacga	tgtcaactta	atgtccttga	caacaaaaag	840
aggacagctc	tgayaaaagg	cgtacaatgc	caggaagatg	aatgtgcggt	aatgttgctg	900
gaacatggca	ctgatccaaa	tattccagat	gagtatggaa	ataccactct	rcactaygct	960
rtctayaatg	aagataaatt	aatggccaaa	gcactgctct	tatayggtgc	tgatatcgaa	1020
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gaaaacactg	aatttgtaaa	aggtaatact	tactattttt	caatttttcc	ctcctaggat	1320
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actccaagaa	aagttaaaca	tgtttcagtg	aatagagatc	ctgctccttt	ggcaagttcc	1440
taaaaaacag	taatagatac	gaggtgatgc	gcctgtcagt	ggcaagggtt	aagatatttc	1500
tgatctcgtg	cc					1512

&lt;210&gt; 369

&lt;211&gt; 1853

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 369

gggtcgccca	ggggsgcgt	gggctttcct	cgggtgggtg	tgggttttcc	ctgggtgggg	60
tgggctgggc	trgaatcccc	tgotggggtt	ggcagggttt	ggctgggatt	gacttttytc	120
ttcaaacaga	ttggaaaccc	ggagttacct	gctagttggt	gaaactgggt	ggtagacgcg	180
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tgggtgctgcc	gttgcttccc	ctgctgcagg	gagagcggca	agagcaacgt	gggcacttct	360
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gaagtagtaa	aactcstgct	ggacagacga	tgtcaactta	atgtccttga	caacaaaaag	840
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gaacatggca	ctgatccaaa	tattccagat	gagtatggaa	ataccactct	rcactaygct	960
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cctatgagac	taggctttga	gaatcaatag	attctttttt	taagaatctt	ttggctagga	1560
gcggtgtctc	acgcctgtaa	ttccagcacc	ttgagaggct	gaggtgggca	gatcacgaga	1620
tcaggagatc	gagaccatcc	tggctaacac	ggtgaaaccc	catctctact	aaaaatacaa	1680
aaacttagct	gggtgtgggtg	gcgggtgcct	gtagtcccag	ctactcagga	rgctgaggca	1740
ggagaatggc	atgaacccgg	gaggtggagg	ttgcagttag	ccgagatccg	ccactacact	1800



120

ccagcctggg tgacagagca agactctgtc tcaaaaaaaaa aaaaaaaaaaaa aaa 1853

<210> 370  
 <211> 2184  
 <212> DNA  
 <213> Homo sapien

<400> 370  
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 aaaaccacct atgacaagcc cacagccaac ataatactaa atggggaaaa gttagaagca 120  
 ttccctctga gaactgcaac aataaataca aggatgctgg attttgtcaa atgccttttc 180  
 tgtgtctgtt gagatgctta tgtgactttg cttttaattc tgtttatgtg attatcacat 240  
 ttattgactt gcctgtgtta gacoggaaga gctggggtgt ttctcaggag ccaccgtgtg 300  
 ctgcggcagc ttcgggataa cttgaggctg catcactggg gaagaaacac aytctgttcc 360  
 gtggcgctga tggctgagga cagagcttca gtgtggcttc tctgcgactg gcttcttcgg 420  
 ggagttcttc cttcatagtt catccatatt gctccagagg aaaattatat tattttgtta 480  
 tggatgaaga gtattacgtt gtgcagatat actgcagtgt cttcatctct tgatgtgtga 540  
 ttgggtaggt tccaccatgt tgccgcagat gacatgattt cagtacctgt gtctggctga 600  
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<210> 371  
 <211> 1855  
 <212> DNA  
 <213> Homo sapien

<220>  
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 <223> n = A,T,C or G

<400> 371  
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&lt;210&gt; 372

&lt;211&gt; 1059

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 372

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&lt;210&gt; 373

&lt;211&gt; 1155

122

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 373

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accagaaata	aataa					1155

&lt;210&gt; 374

&lt;211&gt; 2000

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 374

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123

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aaaaaaaaaa	aaaaaaaaaa					2000

&lt;210&gt; 375

&lt;211&gt; 2040

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 375

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&lt;210&gt; 376

&lt;211&gt; 329

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 376

Met	Asp	Ile	Val	Val	Ser	Gly	Ser	His	Pro	Leu	Trp	Val	Asp	Ser	Phe
1				5					10					15	
Leu	His	Leu	Ala	Gly	Ser	Asp	Leu	Leu	Ser	Arg	Ser	Leu	Met	Ala	Glu

124

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Glu Tyr Thr Ile Val His Ala Ser Phe Ile Ser Cys Ile Ser Ser Ser
      35      40      45
Leu Asp Gly Gln Gly Glu Arg Gln Glu Gln Arg Gly His Phe Trp Arg
      50      55      60
Pro Gln Arg Leu Leu Cys Glu Asp Ala Trp Glu Gln Glu Val Gln Val
      65      70      75      80
Val Leu Pro Leu Leu Pro Leu Leu Gln Gly Ser Gly Lys Ser Asn Val
      85      90      95
Val Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe Met Asp Pro Arg Tyr
      100      105      110
His Val His Gly Glu Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp
      115      120      125
Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp
      130      135      140
Val Asn Lys Arg Asp Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser
      145      150      155      160
Ala Asn Gly Asn Ser Glu Val Val Lys Leu Val Leu Asp Arg Arg Cys
      165      170      175
Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr Ala Leu Thr Lys Ala
      180      185      190
Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly
      195      200      205
Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr
      210      215      220
Ala Val Tyr Asn Glu Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr
      225      230      235      240
Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu
      245      250      255
Leu Gly Ile His Glu Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys
      260      265      270
Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu
      275      280      285
Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile Val Ser Pro Leu Leu
      290      295      300
Glu Gln Asn Val Asp Val Ser Ser Gln Asp Leu Glu Arg Arg Pro Glu
      305      310      315      320
Ser Met Leu Phe Leu Val Ile Ile Met
      325

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<210> 377
<211> 148
<212> PRT
<213> Homo sapien

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<220>
<221> VARIANT
<222> (1)...(148)
<223> Xaa = Any Amino Acid

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<400> 377
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      20      25      30
Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys Xaa Asp Lys
      35      40      45
Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu

```

125

50		55		60
Val Val Lys Leu Xaa Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp				
65		70		75
Asn Lys Lys Arg Thr Ala Leu Xaa Lys Ala Val Gln Cys Gln Glu Asp				
	85		90	
Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro				
	100		105	
Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Xaa Tyr Asn Glu Asp				
	115		120	
Lys Leu Met Ala Lys Ala Leu Leu Tyr Gly Ala Asp Ile Glu Ser				
	130		135	
Lys Asn Lys Val				
145				

&lt;210&gt; 378

&lt;211&gt; 1719

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 378

Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys				
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Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe				
	20		25	
Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp				
	35		40	
His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp				
	50		55	
Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val				
65		70		75
Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn				
	85		90	
Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser				
	100		105	
Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe				
	115		120	
Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His				
	130		135	
Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met				
145		150		155
Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala				
	165		170	
Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val Val Lys Leu Leu				
	180		185	
Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr				
	195		200	
Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met				
	210		215	
Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn				
225		230		235
Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys Leu Met Ala Lys				
	245		250	
Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly				
	260		265	
Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gln Val Val				
	275		280	
Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr				
	290		295	
			300	

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Gly	Arg	Thr	Ala	Leu	Ile	Leu	Ala	Val	Cys	Cys	Gly	Ser	Ala	Ser	Ile
305					310					315					320
Val	Ser	Leu	Leu	Leu	Glu	Gln	Asn	Ile	Asp	Val	Ser	Ser	Gln	Asp	Leu
				325					330					335	
Ser	Gly	Gln	Thr	Ala	Arg	Glu	Tyr	Ala	Val	Ser	Ser	His	His	His	Val
			340					345					350		
Ile	Cys	Gln	Leu	Leu	Ser	Asp	Tyr	Lys	Glu	Lys	Gln	Met	Leu	Lys	Ile
	355					360					365				
Ser	Ser	Glu	Asn	Ser	Asn	Pro	Glu	Asn	Val	Ser	Arg	Thr	Arg	Asn	Lys
370					375					380					
Pro	Arg	Thr	His	Met	Val	Glu	Val	Asp	Ser	Met	Pro	Ala	Ala	Ser	
385				390				395						400	
Ser	Val	Lys	Lys	Pro	Phe	Gly	Leu	Arg	Ser	Lys	Met	Gly	Lys	Trp	Cys
			405					410						415	
Cys	Arg	Cys	Phe	Pro	Cys	Cys	Arg	Glu	Ser	Gly	Lys	Ser	Asn	Val	Gly
			420					425					430		
Thr	Ser	Gly	Asp	His	Asp	Asp	Ser	Ala	Met	Lys	Thr	Leu	Arg	Ser	Lys
		435					440						445		
Met	Gly	Lys	Trp	Cys	Arg	His	Cys	Phe	Pro	Cys	Cys	Arg	Gly	Ser	Gly
450					455					460					
Lys	Ser	Asn	Val	Gly	Ala	Ser	Gly	Asp	His	Asp	Asp	Ser	Ala	Met	Lys
465				470				475						480	
Thr	Leu	Arg	Asn	Lys	Met	Gly	Lys	Trp	Cys	Cys	His	Cys	Phe	Pro	Cys
			485					490						495	
Cys	Arg	Gly	Ser	Gly	Lys	Ser	Lys	Val	Gly	Ala	Trp	Gly	Asp	Tyr	Asp
			500					505					510		
Asp	Ser	Ala	Phe	Met	Glu	Pro	Arg	Tyr	His	Val	Arg	Gly	Glu	Asp	Leu
		515					520					525			
Asp	Lys	Leu	His	Arg	Ala	Ala	Trp	Trp	Gly	Lys	Val	Pro	Arg	Lys	Asp
530					535						540				
Leu	Ile	Val	Met	Leu	Arg	Asp	Thr	Asp	Val	Asn	Lys	Lys	Asp	Lys	Gln
545				550						555					560
Lys	Arg	Thr	Ala	Leu	His	Leu	Ala	Ser	Ala	Asn	Gly	Asn	Ser	Glu	Val
			565					570						575	
Val	Lys	Leu	Leu	Leu	Asp	Arg	Arg	Cys	Gln	Leu	Asn	Val	Leu	Asp	Asn
			580					585					590		
Lys	Lys	Arg	Thr	Ala	Leu	Ile	Lys	Ala	Val	Gln	Cys	Gln	Glu	Asp	Glu
		595					600					605			
Cys	Ala	Leu	Met	Leu	Leu	Glu	His	Gly	Thr	Asp	Pro	Asn	Ile	Pro	Asp
610					615					620					
Glu	Tyr	Gly	Asn	Thr	Thr	Leu	His	Tyr	Ala	Ile	Tyr	Asn	Glu	Asp	Lys
625				630					635					640	
Leu	Met	Ala	Lys	Ala	Leu	Leu	Leu	Tyr	Gly	Ala	Asp	Ile	Glu	Ser	Lys
			645						650					655	
Asn	Lys	His	Gly	Leu	Thr	Pro	Leu	Leu	Gly	Val	His	Glu	Gln	Lys	
			660				665					670			
Gln	Gln	Val	Val	Lys	Phe	Leu	Ile	Lys	Lys	Lys	Ala	Asn	Leu	Asn	Ala
		675					680					685			
Leu	Asp	Arg	Tyr	Gly	Arg	Thr	Ala	Leu	Ile	Leu	Ala	Val	Cys	Cys	Gly
690					695					700					
Ser	Ala	Ser	Ile	Val	Ser	Leu	Leu	Leu	Glu	Gln	Asn	Ile	Asp	Val	Ser
705				710					715					720	
Ser	Gln	Asp	Leu	Ser	Gly	Gln	Thr	Ala	Arg	Glu	Tyr	Ala	Val	Ser	Ser
			725					730					735		
His	His	His	Val	Ile	Cys	Gln	Leu	Leu	Ser	Asp	Tyr	Lys	Glu	Lys	Gln
			740				745					750			
Met	Leu	Lys	Ile	Ser	Ser	Glu	Asn	Ser	Asn	Pro	Glu	Gln	Asp	Leu	Lys
		755					760					765			

Leu Thr Ser Glu Glu Glu Ser Gln Arg Phe Lys Gly Ser Glu Asn Ser  
 770 775 780  
 Gln Pro Glu Lys Met Ser Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp  
 785 790 795 800  
 Arg Glu Val Glu Glu Glu Met Lys Lys His Glu Ser Asn Asn Val Gly  
 805 810 815  
 Leu Leu Glu Asn Leu Thr Asn Gly Val Thr Ala Gly Asn Gly Asp Asn  
 820 825 830  
 Gly Leu Ile Pro Gln Arg Lys Ser Arg Thr Pro Glu Asn Gln Gln Phe  
 835 840 845  
 Pro Asp Asn Glu Ser Glu Glu Tyr His Arg Ile Cys Glu Leu Val Ser  
 850 855 860  
 Asp Tyr Lys Glu Lys Gln Met Pro Lys Tyr Ser Ser Glu Asn Ser Asn  
 865 870 875 880  
 Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Leu  
 885 890 895  
 Glu Gly Ser Glu Asn Gly Gln Pro Glu Leu Glu Asn Phe Met Ala Ile  
 900 905 910  
 Glu Glu Met Lys Lys His Gly Ser Thr His Val Gly Phe Pro Glu Asn  
 915 920 925  
 Leu Thr Asn Gly Ala Thr Ala Gly Asn Gly Asp Asp Gly Leu Ile Pro  
 930 935 940  
 Pro Arg Lys Ser Arg Thr Pro Glu Ser Gln Gln Phe Pro Asp Thr Glu  
 945 950 955 960  
 Asn Glu Glu Tyr His Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe  
 965 970 975  
 Cys Glu Glu Gln Asn Thr Gly Ile Leu His Asp Glu Ile Leu Ile His  
 980 985 990  
 Glu Glu Lys Gln Ile Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser  
 995 1000 1005  
 Leu Ser Cys Lys Lys Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu  
 1010 1015 1020  
 Arg Glu Glu Ile Ala Met Leu Arg Leu Glu Leu Asp Thr Met Lys His  
 1025 1030 1035 1040  
 Gln Ser Gln Leu Pro Arg Thr His Met Val Val Glu Val Asp Ser Met  
 1045 1050 1055  
 Pro Ala Ala Ser Ser Val Lys Lys Pro Phe Gly Leu Arg Ser Lys Met  
 1060 1065 1070  
 Gly Lys Trp Cys Cys Arg Cys Phe Pro Cys Cys Arg Glu Ser Gly Lys  
 1075 1080 1085  
 Ser Asn Val Gly Thr Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr  
 1090 1095 1100  
 Leu Arg Ser Lys Met Gly Lys Trp Cys Arg His Cys Phe Pro Cys Cys  
 1105 1110 1115 1120  
 Arg Gly Ser Gly Lys Ser Asn Val Gly Ala Ser Gly Asp His Asp Asp  
 1125 1130 1135  
 Ser Ala Met Lys Thr Leu Arg Asn Lys Met Gly Lys Trp Cys Cys His  
 1140 1145 1150  
 Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Lys Val Gly Ala Trp  
 1155 1160 1165  
 Gly Asp Tyr Asp Asp Ser Ala Phe Met Glu Pro Arg Tyr His Val Arg  
 1170 1175 1180  
 Gly Glu Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp Gly Lys Val  
 1185 1190 1195 1200  
 Pro Arg Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys  
 1205 1210 1215  
 Lys Asp Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly  
 1220 1225 1230



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Asn Ser Glu Val Val Lys Leu Leu Leu Asp Arg Arg Cys Gln Leu Asn  
 1235 1240 1245  
 Val Leu Asp Asn Lys Lys Arg Thr Ala Leu Ile Lys Ala Val Gln Cys  
 1250 1255 1260  
 Gln Glu Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro  
 1265 1270 1275 1280  
 Asn Ile Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Ile Tyr  
 1285 1290 1295  
 Asn Glu Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp  
 1300 1305 1310  
 Ile Glu Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu Gly Val  
 1315 1320 1325  
 His Glu Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys Lys Lys Ala  
 1330 1335 1340  
 Asn Leu Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu Ile Leu Ala  
 1345 1350 1355 1360  
 Val Cys Cys Gly Ser Ala Ser Ile Val Ser Leu Leu Leu Glu Gln Asn  
 1365 1370 1375  
 Ile Asp Val Ser Ser Gln Asp Leu Ser Gly Gln Thr Ala Arg Glu Tyr  
 1380 1385 1390  
 Ala Val Ser Ser His His His Val Ile Cys Gln Leu Leu Ser Asp Tyr  
 1395 1400 1405  
 Lys Glu Lys Gln Met Leu Lys Ile Ser Ser Glu Asn Ser Asn Pro Glu  
 1410 1415 1420  
 Gln Asp Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Phe Lys Gly  
 1425 1430 1435 1440  
 Ser Glu Asn Ser Gln Pro Glu Lys Met Ser Gln Glu Pro Glu Ile Asn  
 1445 1450 1455  
 Lys Asp Gly Asp Arg Glu Val Glu Glu Glu Met Lys Lys His Glu Ser  
 1460 1465 1470  
 Asn Asn Val Gly Leu Leu Glu Asn Leu Thr Asn Gly Val Thr Ala Gly  
 1475 1480 1485  
 Asn Gly Asp Asn Gly Leu Ile Pro Gln Arg Lys Ser Arg Thr Pro Glu  
 1490 1495 1500  
 Asn Gln Gln Phe Pro Asp Asn Glu Ser Glu Glu Tyr His Arg Ile Cys  
 1505 1510 1515 1520  
 Glu Leu Val Ser Asp Tyr Lys Glu Lys Gln Met Pro Lys Tyr Ser Ser  
 1525 1530 1535  
 Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu Glu Glu  
 1540 1545 1550  
 Ser Gln Arg Leu Glu Gly Ser Glu Asn Gly Gln Pro Glu Lys Arg Ser  
 1555 1560 1565  
 Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp Arg Glu Leu Glu Asn Phe  
 1570 1575 1580  
 Met Ala Ile Glu Glu Met Lys Lys His Gly Ser Thr His Val Gly Phe  
 1585 1590 1595 1600  
 Pro Glu Asn Leu Thr Asn Gly Ala Thr Ala Gly Asn Gly Asp Asp Gly  
 1605 1610 1615  
 Leu Ile Pro Pro Arg Lys Ser Arg Thr Pro Glu Ser Gln Gln Phe Pro  
 1620 1625 1630  
 Asp Thr Glu Asn Glu Glu Tyr His Ser Asp Glu Gln Asn Asp Thr Gln  
 1635 1640 1645  
 Lys Gln Phe Cys Glu Glu Gln Asn Thr Gly Ile Leu His Asp Glu Ile  
 1650 1655 1660  
 Leu Ile His Glu Glu Lys Gln Ile Glu Val Val Glu Lys Met Asn Ser  
 1665 1670 1675 1680  
 Glu Leu Ser Leu Ser Cys Lys Lys Glu Lys Asp Ile Leu His Glu Asn  
 1685 1690 1695

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Ser Thr Leu Arg Glu Glu Ile Ala Met Leu Arg Leu Glu Leu Asp Thr  
 1700 1705 1710  
 Met Lys His Gln Ser Gln Leu  
 1715

<210> 379  
 <211> 656  
 <212> PRT  
 <213> Homo sapien

<400> 379  
 Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys  
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 Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe  
 20 25 30  
 Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp  
 35 40 45  
 His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp  
 50 55 60  
 Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val  
 65 70 75 80  
 Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn  
 85 90 95  
 Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser  
 100 105 110  
 Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe  
 115 120 125  
 Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His  
 130 135 140  
 Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met  
 145 150 155 160  
 Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala  
 165 170 175  
 Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val Val Lys Leu Leu  
 180 185 190  
 Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr  
 195 200 205  
 Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met  
 210 215 220  
 Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn  
 225 230 235 240  
 Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys Leu Met Ala Lys  
 245 250 255  
 Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly  
 260 265 270  
 Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gln Val Val  
 275 280 285  
 Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr  
 290 295 300  
 Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile  
 305 310 315 320  
 Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser Ser Gln Asp Leu  
 325 330 335  
 Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser His His Val  
 340 345 350  
 Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln Met Leu Lys Ile  
 355 360 365  
 Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu

130

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      370      375      380
Glu Glu Ser Gln Arg Phe Lys Gly Ser Glu Asn Ser Gln Pro Glu Lys
385      390      395
Met Ser Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp Arg Glu Val Glu
      405      410      415
Glu Glu Met Lys Lys His Glu Ser Asn Asn Val Gly Leu Leu Glu Asn
      420      425      430
Leu Thr Asn Gly Val Thr Ala Gly Asn Gly Asp Asn Gly Leu Ile Pro
      435      440      445
Gln Arg Lys Ser Arg Thr Pro Glu Asn Gln Gln Phe Pro Asp Asn Glu
      450      455      460
Ser Glu Glu Tyr His Arg Ile Cys Glu Leu Val Ser Asp Tyr Lys Glu
465      470      475      480
Lys Gln Met Pro Lys Tyr Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp
      485      490      495
Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Leu Glu Gly Ser Glu
      500      505      510
Asn Gly Gln Pro Glu Leu Glu Asn Phe Met Ala Ile Glu Glu Met Lys
      515      520      525
Lys His Gly Ser Thr His Val Gly Phe Pro Glu Asn Leu Thr Asn Gly
      530      535      540
Ala Thr Ala Gly Asn Gly Asp Asp Gly Leu Ile Pro Pro Arg Lys Ser
545      550      555      560
Arg Thr Pro Glu Ser Gln Gln Phe Pro Asp Thr Glu Asn Glu Glu Tyr
      565      570      575
His Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe Cys Glu Glu Gln
      580      585      590
Asn Thr Gly Ile Leu His Asp Glu Ile Leu Ile His Glu Glu Lys Gln
      595      600      605
Ile Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser Leu Ser Cys Lys
      610      615      620
Lys Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu Arg Glu Glu Ile
625      630      635      640
Ala Met Leu Arg Leu Glu Leu Asp Thr Met Lys His Gln Ser Gln Leu
      645      650      655

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<210> 380
<211> 671
<212> PRT
<213> Homo sapien

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<400> 380
Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys
1      5      10      15
Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe
      20      25      30
Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp
      35      40      45
His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp
      50      55      60
Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val
65      70      75      80
Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn
      85      90      95
Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser
      100      105      110
Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe
      115      120      125

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Met	Glu	Pro	Arg	Tyr	His	Val	Arg	Gly	Glu	Asp	Leu	Asp	Lys	Leu	His
130						135					140				
Arg	Ala	Ala	Trp	Trp	Gly	Lys	Val	Pro	Arg	Lys	Asp	Leu	Ile	Val	Met
145					150					155					160
Leu	Arg	Asp	Thr	Asp	Val	Asn	Lys	Lys	Asp	Lys	Gln	Lys	Arg	Thr	Ala
				165						170					175
Leu	His	Leu	Ala	Ser	Ala	Asn	Gly	Asn	Ser	Glu	Val	Val	Lys	Leu	Leu
				180						185				190	
Leu	Asp	Arg	Arg	Cys	Gln	Leu	Asn	Val	Leu	Asp	Asn	Lys	Lys	Arg	Thr
				195				200				205			
Ala	Leu	Ile	Lys	Ala	Val	Gln	Cys	Gln	Glu	Asp	Glu	Cys	Ala	Leu	Met
				210				215				220			
Leu	Leu	Glu	His	Gly	Thr	Asp	Pro	Asn	Ile	Pro	Asp	Glu	Tyr	Gly	Asn
225					230						235				240
Thr	Thr	Leu	His	Tyr	Ala	Ile	Tyr	Asn	Glu	Asp	Lys	Leu	Met	Ala	Lys
				245						250					255
Ala	Leu	Leu	Leu	Tyr	Gly	Ala	Asp	Ile	Glu	Ser	Lys	Asn	Lys	His	Gly
				260						265				270	
Leu	Thr	Pro	Leu	Leu	Leu	Gly	Val	His	Glu	Gln	Lys	Gln	Gln	Val	Val
				275				280							
Lys	Phe	Leu	Ile	Lys	Lys	Lys	Ala	Asn	Leu	Asn	Ala	Leu	Asp	Arg	Tyr
				290				295				300			
Gly	Arg	Thr	Ala	Leu	Ile	Leu	Ala	Val	Cys	Cys	Gly	Ser	Ala	Ser	Ile
305					310						315				320
Val	Ser	Leu	Leu	Leu	Glu	Gln	Asn	Ile	Asp	Val	Ser	Ser	Gln	Asp	Leu
				325						330					335
Ser	Gly	Gln	Thr	Ala	Arg	Glu	Tyr	Ala	Val	Ser	Ser	His	His	His	Val
				340					345					350	
Ile	Cys	Gln	Leu	Leu	Ser	Asp	Tyr	Lys	Glu	Lys	Gln	Met	Leu	Lys	Ile
				355				360					365		
Ser	Ser	Glu	Asn	Ser	Asn	Pro	Glu	Gln	Asp	Leu	Lys	Leu	Thr	Ser	Glu
				370				375				380			
Glu	Glu	Ser	Gln	Arg	Phe	Lys	Gly	Ser	Glu	Asn	Ser	Gln	Pro	Glu	Lys
385					390						395				400
Met	Ser	Gln	Glu	Pro	Glu	Ile	Asn	Lys	Asp	Gly	Asp	Arg	Glu	Val	Glu
				405						410					415
Glu	Glu	Met	Lys	Lys	His	Glu	Ser	Asn	Asn	Val	Gly	Leu	Leu	Glu	Asn
				420						425				430	
Leu	Thr	Asn	Gly	Val	Thr	Ala	Gly	Asn	Gly	Asp	Asn	Gly	Leu	Ile	Pro
				435				440					445		
Gln	Arg	Lys	Ser	Arg	Thr	Pro	Glu	Asn	Gln	Gln	Phe	Pro	Asp	Asn	Glu
				450				455				460			
Ser	Glu	Glu	Tyr	His	Arg	Ile	Cys	Glu	Leu	Val	Ser	Asp	Tyr	Lys	Glu
465					470						475				480
Lys	Gln	Met	Pro	Lys	Tyr	Ser	Ser	Glu	Asn	Ser	Asn	Pro	Glu	Gln	Asp
				485						490					495
Leu	Lys	Leu	Thr	Ser	Glu	Glu	Glu	Ser	Gln	Arg	Leu	Glu	Gly	Ser	Glu
				500					505				510		
Asn	Gly	Gln	Pro	Glu	Lys	Arg	Ser	Gln	Glu	Pro	Glu	Ile	Asn	Lys	Asp
				515				520					525		
Gly	Asp	Arg	Glu	Leu	Glu	Asn	Phe	Met	Ala	Ile	Glu	Glu	Met	Lys	Lys
				530								540			
His	Gly	Ser	Thr	His	Val	Gly	Phe	Pro	Glu	Asn	Leu	Thr	Asn	Gly	Ala
545					550						555				560
Thr	Ala	Gly	Asn	Gly	Asp	Asp	Gly	Leu	Ile	Pro	Pro	Arg	Lys	Ser	Arg
				565						570					575
Thr	Pro	Glu	Ser	Gln	Gln	Phe	Pro	Asp	Thr	Glu	Asn	Glu	Glu	Tyr	His
				580						585					590

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Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe Cys Glu Glu Gln Asn  
 595 600 605  
 Thr Gly Ile Leu His Asp Glu Ile Leu Ile His Glu Glu Lys Gln Ile  
 610 615 620  
 Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser Leu Ser Cys Lys Lys  
 625 630 635 640  
 Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu Arg Glu Glu Ile Ala  
 645 650 655  
 Met Leu Arg Leu Glu Leu Asp Thr Met Lys His Gln Ser Gln Leu  
 660 665 670

<210> 381  
 <211> 251  
 <212> DNA  
 <213> Homo sapien

<400> 381  
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 ggtaacatgc ttcccctaag ggtatcccaa cccaggggcc tcacatgac ctctgagggg 120  
 ccaatatccc aggagaagca ttggggaggt gggggcaggt gaaggacca ggactcacac 180  
 atcctggggc tccaaggcag aggagagggt cctcaagaag gtcaggagga aaatccgtaa 240  
 caagcagtca g 251

<210> 382  
 <211> 3279  
 <212> DNA  
 <213> Homo sapiens

<400> 382  
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 atgctggagg gtgtcaggaa gtgatcgggc tctggggcag ggaggagggg tggggagtgt 120  
 cactgggagg ggacatcctg cagaaggtag gagttagcaa acaccgctg caggggaggg 180  
 gagagccctg cggcacctgg gggagcagag ggagcagcac ctgcccaggc ctgggagggg 240  
 gggcctggag ggcgtgagga ggagcgaggg ggctgcatgg ctggagttag ggatcagggg 300  
 cagggcgcgga gatggcctca cacagggaag agaggggccc tctgagagg cctcacctgg 360  
 gccacaggag gacactgctt ttcctctgag gagtacaggag ctgtggatgg tgctggacag 420  
 aagaaggaca gggcctggct caggtgtcca gaggtgtcgt ctggcttccc tttgggatca 480  
 gactgcaggg agggagggcg gcagggttgt ggggggagtg acgatgagga tgacctgggg 540  
 gtggctccag gccttgcccc tgccctgggc ctcacccagc ctccctcaca gtctcctggc 600  
 cctcagtcct tcccctccac tccatcctcc atctggcctc agtgggtcat tctgatcact 660  
 gaactgacca taccagccc tgcccacggc cctccatggc tcccgaatgc cctggagagg 720  
 ggacatctag tcagagagta gtccctgaaga ggtggcctct gcgatgtgcc tgtgggggca 780  
 gcacactgca gatggtcccg gccctcatcc tgctgacctg tctgcaggga ctgtcctcct 840  
 ggaccttgcc ccttgtgcag gagctggacc ctgaagtccc ctcccatag gccaaagactg 900  
 gagccttggt cctctgttg gactccctgc ccatattctt gtgggagtgg gttctggaga 960  
 catctctgtc tgttcctgag agctgggaat tgcctcagc catctgcctg cgcggttctg 1020  
 agagatggag ttgcctaggc agttattggg gccaatcttt ctactgtgt ctctcctcct 1080  
 ttacccttag ggtgattctg ggggtccact tgtctgtaat ggtgtgtctc aaggtatcac 1140  
 atcatggggc cctgagccat gtgccctgcc tgaagaagcct gctgtgtaca ccaaggtggg 1200  
 gcattaccgg aagtggatca aggacaccat cgcagccaac ccctgagtgc ccctgtccca 1260  
 ccctacctc tagtaaatat aagtccacct cacgttctgg catcacttgg cctttctgga 1320  
 tgctggacac ctgaagcttg gaactcaact ggccgaagct cgagcctcct gagtccctact 1380  
 gacctgtgct ttctgggtgt gagtccaggg ctgctaggaa aaggaatggg cagacacagg 1440  
 tgtatgcaa tgtttctgaa atgggtataa tttcgtctc tccttcggaa cactggctgt 1500  
 ctctgaagac ttctcgctca gtttcagtga ggacacacac aaagacgtgg gtgacctgt 1560  
 tgtttgtggg gtgcagagat gggaggggtg gggccacccc tggagagtg gacagtga 1620  
 caaggtggac actctctaca gatcactgag gataagctgg agccacaatg catgaggcac 1680  
 acacacagca aggttgacgc tgtaaacata gccacgctg tcctgggggc actgggaagc 1740

```
<210> 383
<211> 154
<212> PRT
<213> Homo sapiens
```

```
<210> 384
<211> 557
<212> DNA
<213> Homo sapiens
```

&lt;400&gt; 384

```
ggatcctcta gagcgccgc ctactactac taaattcgcg gccgcgtcga cgaagaagag 60
aaagatgtgt ttgttttgg actctctgtg gtcccttoca atgctgtggg ttccaacca 120
ggggaagggt cccttttgca ttgccaagt ccataacat gagcactact ctaccatgg 180
tctgcctcct ggccaagcag gctggtttgc aagaatgaaa tgaatgattc tacagctagg 240
acttaacctt gaaatggaaa gtcttgcaat cccatttgca ggatccgtct gtgcacatgc 300
ctctgtagag agcagcattc ccaggacctc tggaaacagt tggcactgta aggtgcttgc 360
tccccaagac acatcctaaa aggtgttgta atggtgaaaa cgtcttcctt ctttattgcc 420
ccttcttatt tatgtgaaca actgtttgtc tttttttgta tcttttttaa actgtaaagt 480
tcaattgtga aaatgaatat catgcaaata aattatgcga ttttttttcc aaagtaaaaa 540
aaaaaaaaa aaaaaaa 557
```

&lt;210&gt; 385

&lt;211&gt; 337

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 385

```
ttcccagggtg atgtgcgagg gaagacacat ttactatcct tgatgggggt gattccttta 60
gtttctctag cagcagatgg gttaggagga agtgaccaa gtggttgact cctatgtgca 120
tctcaagacc atctgctgtc ttcgagtacg gacacatcat cactcctgca ttgttgatca 180
aaacgtggag gtgcttttcc tcagctaaga agcccttagc aaaagctcga atagacttag 240
tatcagacag gtccagtttc cgcaccaaca cctgctggtt cctgtcgtg gtctggatct 300
ctttggccac caattcccc tttccacat cccggca 337
```

&lt;210&gt; 386

&lt;211&gt; 300

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 386

```
gggcccgcta ccggcccagg cccgcctcg cgagtcctcc tccccgggtg cctgcccgca 60
gcccgctcgg ccagaggggt gggcgcgagg ctgcctctac cggtggcgg ctgtaactca 120
gcgaccttgg ccgaaggct ctagcaagga ccaccgacc ccagccggcg cggcgcgggc 180
gcggactttg ccggtgtgt gggcgggagc ggactgcgtg tccgcggacg ggcagcgaag 240
atgttagcct tcgctgccag gaccgtggac cgatcccagg gctgtggtgt aacctcagcc 300
```

&lt;210&gt; 387

&lt;211&gt; 537

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 387

```
gggccgagtc gggcaccaag ggactctttg caggcttctc tcctcggatc atcaaggctg 60
ccccctcctg tgccatcatg atcagcacct atgagttcgg caaaagcttc ttccagaggc 120
tgaaccagga ccggtctctg ggcggtgaa aggggcaagg aggcaaggac cccgtctctc 180
ccacggatgg ggagagggca ggaggagacc cagccaagt ccttttctc agcactgagg 240
gagggggctt gtttcccttc cctcccgcg acaagctcca gggcagggt gtccctctgg 300
gcggcccagc acttctcag acacaacttc ttctgctgc tccagtctg gggatcatca 360
cttaccacc cccaagtgc aagacaaat cttccagctg ccccttctg gtttccctgt 420
gtttgctgta gctgggcatg tctccaggaa ccaagaagcc ctgagcctgg tgtagtctcc 480
ctgacccttg ttaattcctt aagtctaag atgatgaact tcaaaaaaa aaaaaaa 537
```

&lt;210&gt; 388

&lt;211&gt; 520

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

135

```

<400> 388
aggataatatt ttaaaccaat caaatgaaaa aaacaaacaa acaaaaaagg aaatgtcatg 60
tgaggttaaa ccagtttgca ttcccctaatt gtggaaaaag taagaggact actcagcact 120
gtttgaagat tgcctcttct acagcttctg agaatttgtt tatttcactt gccaaagtga 180
ggacccccct cccaacatgc ccagcccac ccctaagcat ggtcccttgt caccaggcaa 240
ccaggaaact gctacttggt gacctacca gagaccagga gggtttggtt agctcacagg 300
acttccccca cccagaaga ttagcatccc atactagact cataactcaac tcaactaggc 360
tcatactcaa ttgatggta ttagacaatt ccatttcttt ctggttatta taaacagaaa 420
atctttcttc ttctcattac cagtaaaggc tcttggtatc tttctggttg aatgatttct 480
atgaacttgt cttattttta tgggtgggtt ttttcttggt 520

```

```

<210> 389
<211> 365
<212> DNA
<213> Homo sapiens

```

```

<400> 389
cgttgcccca gtttgacaga aggaaaggcg gagcttattc aaagtctaga gggagtggag 60
gagttaaggc tggatttcag atctgcctgg ttccagccgc agtgtgccct ctgctcccc 120
aacgactttc caaataatct caccagcgcc ttccagctca ggcgtcctag aagcgtcttg 180
aagcctatgg ccagctgtct ttgtgttccc tctcaccgcg ctgtcctcac agctgagact 240
cccaggaaac cttcagacta ccttcctctg ccttcagcaa ggggcgttgc ccacattctc 300
tgagggtcag tggaagaacc tagactccca ttgctagagg tagaaagggg aaggggtgctg 360
gggag 365

```

```

<210> 390
<211> 221
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(221)
<223> n = A,T,C or G

```

```

<400> 390
tgcctctcca tcctggcccc gacttctctg tcaggaaaagt ggggatggac cccatctgca 60
tacacggntt ctcatgggtg tggaacatct ctgcttgcgg ttccaggaag gcctctggct 120
gctctangag tctgancnga ntcgttgccc cantntgaca naaggaaagg cggagcttat 180
tcaaagtcta gagggagtgg aggagttaag gctggatttc a 221

```

```

<210> 391
<211> 325
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(325)
<223> n = A,T,C or G

```

```

<400> 391
tgagcaggt cccgaggcct ccctagagcc tggggccgac tctgtgncga tgcangcttt 60
ctctcgcgcc cagcctggag ctgctcctgg catctaccaa caatcagncg aggcgagcag 120
tagccagggc actgctgcca acagccagtc cnnataccat catgtnaccc ggtgngctct 180
naantngat ntccanagcc ctacccatcn tagttctgct ctcccaccgg ntaccagccc 240
cactgcccag gaatcctaca gccagtaccc tgtcccgcag tctctaccta ccagtacgat 300

```



136

gagacctccg gctactacta tgacc

325

&lt;210&gt; 392

&lt;211&gt; 277

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(277)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 392

```

atattgttta actccttcct ttatatcttt taacattttc atggngaaa gttcacatct 60
agtctcactt nggcnagn gn ctcctacttg agtctcttcc ccggcctggn ccagtngnaa 120
antaccanga accgncatgn cttanaa nccgtggttn tgggttnntc aatgactgca 180
tgcaatgcac caccctgtcc actacgtgat gctgtaggat taaagtctca cagtgggcgg 240
ctgaggatac agcgccgcgt cctgtgttgc tggggaa 277

```

&lt;210&gt; 393

&lt;211&gt; 566

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 393

```

actagtccag tgtggtggaa ttgcggccg cgtcgacgga caggtcagct gtctggctca 60
gtgatctaca ttctgaagtt gtctgaaaat gtcttcatga ttaaattcag cctaaacgtt 120
ttgccgggaa cactgcagag acaatgtgtg gagtttccaa ccttagccca tctgcgggca 180
gagaaggtct agtttgtcca tcagcattat catgatata ggactggtta cttggttaag 240
gaggggtcta ggagatctgt cccttttaga gacaccttac ttataatgaa gtatttgga 300
gggtggtttt caaaagtaga aatgtcctgt attccgatga tcacctctga aacattttat 360
cattatttaa tcacccctgc ctgtgtctat tattatattc atatctctac gctggaaact 420
ttctgcctca atgtttactg tgccttctgt tttgctagtt tgtgttcttg aaaaaaaaaa 480
cattctctgc ctgagtttta atttttgtcc aaagttattt taatctatac aattaaaagc 540
tttgcctat caaaaaaaaa aaaaaa 566

```

&lt;210&gt; 394

&lt;211&gt; 384

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(384)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 394

```

gaacatacat gtcccgccac ctgagctgca gtctgacatc atcgccatca cgggcctcgc 60
tgcaaatng gaccgggcca aggctggact gctggagcgt gtgaaggagc tacaggccna 120
gcaggaggac cgggctttaa ggagttttaa gctgagtgtc actgtagacc ccaaatacca 180
tccaagatt atcgggagaa agggggcagt aattaccaa atccggttg agcatgacgt 240
gaacatccag tttctgata aggacgatgg gaaccagccc caggaccaa ttaccatcac 300
agggtacgaa aagaacacag aagctgccag gtagctata ctgagaattg tgggtgaact 360
tgagcagatg gtttctgagg acgt 384

```

&lt;210&gt; 395

&lt;211&gt; 399

&lt;212&gt; DNA

137

&lt;213&gt; Homo sapiens

&lt;400&gt; 395

```
ggcaaaactg tgtgacctca ataagacctc gcagatccaa ggtcaagtat cagaagtgc 60
tctgaccttg gactccaaga cctacatcaa cagcctggct atattagatg atgagccagt 120
tatcagaggt ttcattcattg cggaaattgt ggagtctaag gaaatcatgg cctctgaagt 180
attcacgtct ttccagtacc ctgagttctc tatagagttg cctaacacag gcagaattgg 240
ccagctactt gtctgcaatt gtatcttcaa gaataccctg gccatccctt tgactgacgt 300
caagttctct ttggaaagcc tgggcatctc ctactacag acctctgacc atgggacggg 360
gcagcctggg gagaccatcc aatcccaaat aaaatgcac 399
```

&lt;210&gt; 396

&lt;211&gt; 403

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(403)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 396

```
tggagttntc agtgcaaaca agccataaag ctccagtagc aaattactgt ctccacagaaa 60
gacattttca acttctgctc cagctgctga taaaacaaat catgtgttta gcttgactcc 120
agacaaggac aacctgttcc ttcataactc tctagagaaa aaaaggagtt gttagtagat 180
actaaaaaaaa gtggatgaat aatctggata tttttcctaa aaagattcct tgaaacacat 240
taggaaaatg gagggcctta tgatcagaat gctagaatta gtccattgtg ctgaagcagg 300
gttttagggga gggagtgagg gataaaagaa ggaaaaaaag aagagtgaga aaacctattt 360
atcaaagcag gtgctatcac tcaatgttag gccctgctct ttt 403
```

&lt;210&gt; 397

&lt;211&gt; 100

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(100)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 397

```
actagtnacg tgtggtggaa ttcgcggccg cgtcgacctc naanccatct ctatagcaaa 60
tccatccccg ctctggttg gtnacagaat gactgacaaa 100
```

&lt;210&gt; 398

&lt;211&gt; 278

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(278)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 398

```
gcggccgcgt cgacagcagt tccgccagcg ctgcgccctg ggtgggggatg tgctgcacgc 60
ccacctggac atctggaagt cagcggcctg gatgaaagag cggacttcac ctggggcgat 120
tcactactgt gcctcgacca gtgaggagag ctggaccgac agcgaggtag actcatcatg 180
```

138

ctccgggcag cccatccacc tgtggcagtt cctcaaggag ttgctactca agccccacag 240  
 ctatggccgc ttcattangt ggctcaacaa ggagaagg 278

<210> 399  
 <211> 298  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(298)  
 <223> n = A,T,C or G

<400> 399  
 acggaggtgg aggaagcgnc cctgggatcg anaggatggg tctgncatt gaccncctcn 60  
 ggggtgccng catggagcgc atgggcgcgg gcctgggcca cggcatggat cgcgtgggct 120  
 ccgagatcga gcgcatgggc ctggatcatgg accgcatggg ctccgtggag cgcgtgggct 180  
 ccggcattga gcgcatgggc ccgctgggccc tcgaccacat ggcctccanc attgancgca 240  
 tgggccaagac catggagcgc attggctctg gcgtggagcn catgggtgcc ggcatggg 298

<210> 400  
 <211> 548  
 <212> DNA  
 <213> Homo sapiens

<400> 400  
 acatcaacta cttcctcatt ttaaggtatg gcagttccct tcatccctt ttcctgcctt 60  
 gtacatgtac atgtatgaaa tttccttctc ttaccgaact ctctccacac atcacaaggt 120  
 caaagaacca cacgcttaga agggtaagag ggcaccctat gaaatgaaat ggtgatttct 180  
 tgagtctctt ttttccacgt ttaaggggcc atggcaggac ttagagttgc gagttaagac 240  
 tgcagagggc tagagaatta tttcatacag gctttgaggc caccatgtc acttatcccg 300  
 tataccctct caccatcccc ttgtctactc tgatgcccc aagatgcaac tgggcagcta 360  
 gttggcccca taattctggg cctttgttgt ttgttttaac tacttgggca tccaggaag 420  
 ctttccagtg atctctacc atgggcccc ctccctggg atagccccct ccaggccctg 480  
 tccccagccc ctctgcccc agcccacccg cttgccttgg tgctcagccc tcccattggg 540  
 agcaggtt 548

<210> 401  
 <211> 355  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(355)  
 <223> n = A,T,C or G

<400> 401  
 actgtttcca tggtatgttt ctacacattg ctacctcagt gctcctggaa acttagcttt 60  
 tgatgtctcc aagtagtcca ccttcattta actctttgaa actgtatcat ctttgccaag 120  
 taagagtggg ggcctatttc agctgcttg acaaaatgac tggctcctga cttaacgttc 180  
 tataaatgaa tgtgctgaag caaagtggcc atggtggcgg cgaagaagan aaagatgtgt 240  
 tttgttttgg actctctgtg gtcccttcca atgctgnngg tttccaacca ggggaaggg 300  
 cccttttgca ttgccaagtg ccataacat gagcactact ctaccatggn tctgc 355

<210> 402  
 <211> 407  
 <212> DNA

139

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(407)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 402

```

atggggcaag ctggataaag aaccaagacc cactggagta tgctgtcttc aagaaaccca 60
tctcacatgc ggtggcatac ataggctcaa aataaaggaa tggagaaaaa tatttcaagc 120
aaatggaaaa cagaaaaaag cagggtgttc actcctactt tctgacaaaa cagactatgc 180
gaataaagat aaaaaagaga aggacattac aaagggtggtc ctgacctttg ataaatctca 240
ttgcttgata ccaacctggg ctgttttaat tgcccaaacc aaaaggataa tttgctgagg 300
ttgtggagct tctcccctgc agagagtccc tgatctccca aaatttggtt gagatgtaag 360
gntgattttg ctgacaactc cttttctgaa gttttactca tttccaa 407

```

&lt;210&gt; 403

&lt;211&gt; 303

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(303)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 403

```

cagtatttat agccnaactg aaaagctagt agcaggcaag tctcaaattc aggcacccaa 60
tcctaagcaa gagcctatggc atggtgaaaa tgcaaaagga gagtctggcc aatctacaaa 120
tagagaacaa gacctactca gtcattgaaca aaaaggcaga caccaacatg gatctcatgg 180
gggattggat attgtaatta tagagcagga agatgacagt gatcgtcatt tggcacaaca 240
tcttaacaac gaccgaaacc cattattttac ataaacctcc attcggtaac catgttgaaa 300
gga 303

```

&lt;210&gt; 404

&lt;211&gt; 225

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 404

```

aagtgttaact tttaaaaatt tagtggattt tgaaaattct tagaggaaaag taaaggaaaa 60
attgttaatg cactcattta cctttacatg gtgaaagtgc tctcttgatc ctacaaacag 120
acattttcca ctctgtgttc catagtgtgt aagtgtatca gatgtgttgg gcatgtgaat 180
ctccaagtgc ctgtgtaata aataaagtat ctttatttca ttcatt 225

```

&lt;210&gt; 405

&lt;211&gt; 334

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(334)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 405

```

gagctgttat actgtgagtt ctactaggaa atcatcaaatt ctgagggttg tctggaggac 60
ttcaatacac ctccccccat agtgaatcag cttccagggg gtccagtccc tctccttact 120

```

140

```

tcatcccat cccatgcaa aggaagacc tccctccttg gctcacagcc ttctctaggc 180
ttccagtgct ctccaggaca gagtgggtta tgttttcagc tccatccttg ctgtgagtgt 240
ctggtgcggt tgtgcctcca gcttctgctc agtgcttcat ggacagtgtc cagcccatgt 300
cactctccac tctctcannng tggatcccac ccct 334

```

```

<210> 406
<211> 216
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(216)
<223> n = A,T,C or G

```

```

<400> 406
tttcatacct aatgagggag ttganatnac atnnaaccag gaaatgcatg gatctcaang 60
gaaacaaaca cccaataaac tcggagtggc agactgacaa ctgtgagaca tgcacttgct 120
acnaaacaca aatttnatgt tgcacccttg tttctacacc tgtgggttat gacaaagaca 180
actgccaaag aatnttcaag aaggaggact gccant 216

```

```

<210> 407
<211> 413
<212> DNA
<213> Homo sapiens

```

```

<400> 407
gctgacttgc tagtatcatc tgcattcatt gaagcacaag aacttcatgc cttgactcat 60
gtaaatgcaa taggattaaa aaataaattt gatatcacat ggaaacagac aaaaaatatt 120
gtacaacatt gcaccagtg tgcagattcta cacctggcca ctccaggaagc aagagttaat 180
cccagaggtc tatgtcctaa tgtgttatgg caaatggatg tcatgcacgt accttcattt 240
ggaaaattgt catttgtcca tgtgacagtt gatacttatt cacatttcat atgggcaacc 300
tgccagacag gagaaagtct tcccattgta aaagacattt attatcttgt tttcctgtca 360
tgggagttcc agaaaaagtt aaaacagaca atgggccagg ttctgtagta aag 413

```

```

<210> 408
<211> 183
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(183)
<223> n = A,T,C or G

```

```

<400> 408
ggagctngcc ctcaattcct ccatntctat gttancatat ttaatgtctt ttgnnattaa 60
tncttaacta gttaatcctt aaagggtan ntaatcctta actagtccct ccattgtgag 120
cattatcctt ccagtattcn ccttctnttt tatttactcc ttcttggtta cccatgtact 180
ntt 183

```

```

<210> 409
<211> 250
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature

```

141

&lt;222&gt; (1)...(250)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 409

```

cccacgcatg ataagctctt tatttctgta agtcctgcta ggaaatcatc aaatctgacg 60
gtgggtttggg ggacctgaac aaacctcctg taattaatca gctttcagtt totcccccta 120
gtccctcctt caacaacata ggaggatcct ccccttcttt ctgctcacgg ccttatctag 180
gcttcccagt gccccagga cagcgtgggc tatgtttaca ggcntcctt gctggggggg 240
ggcctatgc                                     250

```

&lt;210&gt; 410

&lt;211&gt; 306

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(306)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 410

```

ggctggtttg caagaatgaa atgaatgatt ctacagctag gacttaacct tgaaatggaa 60
agtcttgcaa tcccatttgc aggatccgtc tgtgcacatg cctotgtaga gagcagcatt 120
cccagggacc ttggaaacag ttggcactgt aagggtgctt ctccccaaaga cacatcctaa 180
aagggtgttg aatggtgaaa accgcttcct tctttattgc ccttcttat ttatgtgaac 240
nactggttgg ctttttttgn atctttttta aactggaaaag ttcaattgng aaaatgaata 300
tcntgc                                     306

```

&lt;210&gt; 411

&lt;211&gt; 261

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(261)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 411

```

agagatattn cttaggtnaa agttcataga gttcccatga actatatgac tggccacaca 60
ggatcttttg tatttaagga ttctgagatt ttgcttgagc aggattagat aaggctgttc 120
tttaaatgtc tgaaatggaa cagatttcaa aaaaaaaccc cacaatctag ggtgggaaca 180
aggaaggaaa gatgtgaata ggctgatggg caaaaaacca atttaccat cagttccagc 240
cttctctcaa ggngaggcaa a                                     261

```

&lt;210&gt; 412

&lt;211&gt; 241

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(241)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 412

```

gttcaatgtt acctgacatt tctacaacac ccactcacc gatgtattcg ttgccagtg 60
ggaacatacc agcctgaatt tggaaaaaat aattgtgttt ctgcccagc aaatactacg 120

```

142

actgactttg atggctccac aaacataacc cagtgtaaaa acagaagatg tggaggggag 180  
 ctgggagatt tcaactgggta cattgaattc ccaaactacc cangcaatta cccagccaac 240  
 a 241

<210> 413  
 <211> 231  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(231)  
 <223> n = A,T,C or G

<400> 413  
 aactcttaca atccaagtga ctcactctgtg tgcttgaatc ctttccactg tctcatctcc 60  
 ctcactccaag tttctagtag cttctctttg ttgtgaagga taatcaaact gaacaacaaa 120  
 aagtttactc tcctcatttg gaacctaaaa actctcttct tcctgggtct gagggctcca 180  
 agaatccttg aatcanttct cagatcattg gggacaccan atcaggaacc t 231

<210> 414  
 <211> 234  
 <212> DNA  
 <213> Homo sapiens

<400> 414  
 actgtccatg aagcactgag cagaagctgg aggcacaacg caccagacac tcacagcaag 60  
 gatggagctg aaaacataac ccactctgtc ctggaggcac tgggaagcct agagaaggct 120  
 gtgagccaag gagggagggt cttcctttgg catgggatgg ggatgaagta aggagaggga 180  
 ctggaccccc tggaagctga ttcactatgg ggggaggtgt attgaagtcc tcca 234

<210> 415  
 <211> 217  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(217)  
 <223> n = A,T,C or G

<400> 415  
 gcataggatt aagactgagt atcttttcta cattctttta actttctaag gggcactttct 60  
 caaaacacag accaggtagc aaatctccac tgctctaagg ntctaccac cactttctca 120  
 cacctagcaa tagtagaatt cagtcctact tctgaggcca gaagaatggt tcagaaaaat 180  
 antggattat aaaaaataac aattaagaaa aataatc 217

<210> 416  
 <211> 213  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(213)  
 <223> n = A,T,C or G

<400> 416

143

```

atgcataatnt aaagganact gcctcgcttt tagaagacat ctggngctgct ctctgcatga 60
ggcacagcag taaagctctt tgattcccag aatcaagaac tctccccttc agactattac 120
cgaatgcaag gtggttaatt gaaggccact aattgatgct caaatagaag gatattgact 180
atattggaac agatggagtc tctactacaa aag                                     213

```

```

<210> 417
<211> 303
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(303)
<223> n = A,T,C or G

```

```

<400> 417
nagtcttcag gcccatcagg gaagttcaca ctggagagaa gtcatacata tgtactgtat 60
gtgggaaagg ctttactctg agttcaaadc ttcaagccca tcagagagtc cacactggag 120
agaagccata caaatgcaat gagtgtggga agagcttcag gagggattcc cattatcaag 180
ttcatctagt ggtccacaca ggagagaaac cctataaatg tgagatatgt gggaagggct 240
tcantcaaag ttcgtatctt caaatccatc ngaaggncca cagtatanan aaacctttta 300
agt                                             303

```

```

<210> 418
<211> 328
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(328)
<223> n = A,T,C or G

```

```

<400> 418
tttttgccg tgggtggggca gggacggggac angagtctca ctctgttgcc caggctggag 60
tgcacaggca tgatctcggc tcaactacaac ccctgcctcc catgtccaag cgattcttgt 120
gcctcagcct tccctgtagc tagaattaca ggcacatgcc accacaccca gctagttttt 180
gtatttttag tagagacagg gtttcaccaa gttggccagg ctggtctcaa actcctnacc 240
tcagnggtca ggctggtctc aaactcctga cctcaagtga tctgcccacc tcagcctccc 300
aaagtgtctan gattacaggc cgtgagcc                                     328

```

```

<210> 419
<211> 389
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(389)
<223> n = A,T,C or G

```

```

<400> 419
cctcctcaag acggcctgtg gtccgcctcc cggcaaccaa gaagcctgca gtgocatatg 60
acccttgagc catggactgg agcctgaaag gcagcgtaaa cctgtctcct gatcttctgt 120
cttgtttcct ctctgtggct ccattcatag cacagttggt gcaactgagg ttgtgcaggc 180
cgagcaaggc caagctggct caaagagcaa ccagtcactc ctgccacggg gtgccaggca 240
ccggttctcc agccaccaac ctcaactcgt cccgcaaagt gcacatcagt tcttctaccc 300
taaaggtagg accaaagggc atctgctttt ctgaagtcct ctgctctatc agccatcacg 360

```



144

tggcagccac tcnggctgtg tcgacgcgg

389

&lt;210&gt; 420

&lt;211&gt; 408

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 420

```

gttcctccta actcctgcca gaaacagctc tcctcaacat gagagctgca cccctcctcc 60
tgccagggc agcaagcctt agccttggt tcttgtttct gcttttttcc tggctagacc 120
gaagtgtact agccaaggag ttgaagtttg tgactttggt gtttcggcat ggagaccgaa 180
gtccattga cacctttccc actgaccca taaaggaatc ctcatggcca caaggatttg 240
gccaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
gatatagaaa attcctgaat gagtccata aacatgaaca ggtttatatt cgaagcacag 360
acgttgaccg gactttgatg aagtgcctatg acaaacctgg caagcccg 408

```

&lt;210&gt; 421

&lt;211&gt; 352

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(352)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 421

```

gtcaaaaat ctttttactg atnggcatgg ctacacaatc attgactatt acggaggcca 60
gaggagaatg aggctggcc tgggagccct gtgcctacta naagcacatt agattatcca 120
ttcactgaca gaacaggtct tttttgggtc cttcttctcc accacnatat acttgacgtc 180
ctccttcttg aagattcttt ggcagttgtc tttgtcataa cccacaggtg tagaaacaag 240
ggtgcaacat gaaatctctg tttcgtagca agtgcatgtc tcacaagttg gcangtctgc 300
cactccgagt ttattgggtg tttgtttcct ttgagatcca tgcatttctt gg 352

```

&lt;210&gt; 422

&lt;211&gt; 337

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 422

```

atgccaccat gctggcaatg cagcgggcgg tcgaaggcct gcatatccag cccaagctgg 60
cgatgatcga cggcaaccgt tgcccgaagt tgccgatgcc agccgaagcg gtggtcaagg 120
gcgatagcaa ggtgccggcg atcgcgcgcg cgtcaatcct ggccaaggtc agccgtgatc 180
gtgaaatggc agctgtcgaa ttgatctacc cgggttatgg catcggcggg cataagggtc 240
atccgacacc ggtgcacctg gaagccttgc agcggctggg gccgacgcg attcaccgac 300
gcttcttccg ccggtacggc tggcctatga aaattat 337

```

&lt;210&gt; 423

&lt;211&gt; 310

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(310)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 423

145

```

gctcaaaaat ctttttactg atatggcatg gctacacaat cattgactat tagaggccag 60
aggagaatga ggccctggcct gggagccctg tgcctactan aagcncatta gattatccat 120
tcaactgacag aacagggtctt ttttgggtcc ttcttctcca ccacgatata cttgcagtc 180
tccttcttga agattctttg gcagttgtct ttgtcataac ccacagggtg anaacaagg 240
gtgcaacatg aaatttctgt ttcgtagcaa gtgcatgtct cacagttgtc aagtctgccc 300
tccgagttta                                     310

```

&lt;210&gt; 424

&lt;211&gt; 370

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(370).

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 424

```

gctcaaaaat ctttttactg ataggcatgg ctacacaatc attgactatt agaggccaga 60
ggagaatgag gcctggcctg ggagccctgt gcctactaga agcacattag attatccatt 120
cactgacaga acagggtctt tttgggtcct ttcttctccac cacgatatac ttgcagtcct 180
ccttcttgaa gattcttttg cagttgtctt tgtcataacc cacagggtgta gaaacatcct 240
ggttgaatct cctggaactc cctcattagg tatgaaatag catgatgcat tgcataaagt 300
cacgaagggt gcaaagatca caacgctgcc cagganaaca ttcatgtgta taagcaggac 360
tccgtcgacg                                     370

```

&lt;210&gt; 425

&lt;211&gt; 216

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(216)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 425

```

aattgctatn ntttattttg ccaactcaaaa taattaccaa aaaaaaaaaa tnttaaata 60
taacaacnca acatcaaggn aananaaca ggaatggntg actntgcata aatnggccga 120
anattatcca ttatnttaag ggttgacttc aggnatagc acacagacaa acatgcccag 180
gaggnnttca ggaccgctcg atgtnttntg aggagg                                     216

```

&lt;210&gt; 426

&lt;211&gt; 596

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 426

```

cttcagtgga ggataaccct gttgccccgg gccgagggtc tccattaggc totgattgat 60
tggcagtcag tgatggaagg gtgttctgat cattccgact gcccgaaggg tcgctggcca 120
gctctctgtt ttgctgagtt ggcagtagga cctaatttgt taattaagag tagatggtga 180
gctgtccttg tattttgatt aacctaatgg ccttcccagc acgactcgga ttcagctgga 240
gacatcacgg caacttttaa tgaaatgatt tgaagggccca ttaagaggca cttcccgtta 300
ttaggcagtt catctgcact gataacttct tggcagctga gctggtcgga gctgtggccc 360
aaacgcacac ttggcttttg gttttgagat acaactctta atcttttagt catgcttgag 420
ggtggatggc cttttcagct ttaacccaat ttgcactgcc ttggaagtgt agccaggaga 480
atacactcat atactcgtgg gotttagaggc cacagcagat gtcattggtc tactgcctga 540
gtcccgtggt tcccatccca ggaccttcca tcggcgagta cctgggagcc cgtgct      596

```

146

<210> 427  
 <211> 107  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(107)  
 <223> n = A,T,C or G

<400> 427  
 gaagaattca agttaggttt attcaaaggg cttacngaga atcctanacc caggncccag 60  
 cccgggagca gccttanaga gtcctgttt gactgccggg ctcagng 107

<210> 428  
 <211> 38  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(38)  
 <223> n = A,T,C or G

<400> 428  
 gaacttocna anaangactt tattcactat ttacatt 38

<210> 429  
 <211> 544  
 <212> DNA  
 <213> Homo sapiens

<400> 429  
 ctttgctgga cggaataaaa gtggacgcaa gcatgacctc ctgatgaggg cgctgcattt 60  
 attgaagagc ggctgcagcc ctgcggttca gattaaaatc cgagaattgt atagacgccg 120  
 atatccacga actcttgaag gactttctga tttatocaca atcaaatcat cggttttcag 180  
 tttggatggt ggctcatcac ctgtagaacc tgacttggcc gtggctggaa tccactogtt 240  
 gccttccact tcagttacac ctcaactcacc atcctctcct gttggttctg tgcgtcttca 300  
 agatactaag cccacatttg agatgcagca gccatctccc ccaattcctc ctgtccatcc 360  
 tgatgtgcag ttaaaaaatc tgccctttta tgatgtcctt gatgttctca tcaagcccac 420  
 gagtttagtt caaagcagta ttcagcgatt tcaagagaag ttttttattt ttgctttgac 480  
 acctcaacaa gtttagagaga tatgcataac cagggatttt ttgccagggtg gtaggagaga 540  
 ttat 544

<210> 430  
 <211> 507  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(507)  
 <223> n = A,T,C or G

<400> 430  
 cttatcncaa tgggggtccc aaacttggct gtgcagtggg aactccgggg gaattttgaa 60  
 gaacactgac acccatcttc caccgccgaca ctctgattta attgggctgc agtgagaaca 120

147

```

gagcatcaat ttaaaaagct gccagaatg ttntoctggg cagcgttggt atctttgccn 180
ccttcgtgac tttatgcaat gcatcatgct atttcatacc taatgaggga gttccaggag 240
attcaaccag gatgtttcta cncctgtggg ttatgacaaa gacaactgcc aaagaatntt 300
caagaaggag gactgcaagt atatcgtggg ggagaagaag gacccaaaaa agacctgttc 360
tgtcagtga tggataatct aatgtgcttc tagtaggcac agggctccca ggccaggcct 420
cattctcttc tggcctctaa tagtcaatga ttgtgtagcc atgcctatca gtaaaaagat 480
ttttgagcaa aaaaaaaaaa aaaaaaa 507

```

```

<210> 431
<211> 392
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(392)
<223> n = A,T,C or G

```

```

<400> 431
gaaaattcag aatggataaa aacaaatgaa gtacaaaata tttcagattt acatagcgat 60
aaacaagaaa gcacttatca ggaggactta caaatggaag tacactctan aaccatcatc 120
tatcatggct aaatgtgaga ttagcacagc tgtattattt gtacattgca aacacctaga 180
aagagatggg aaacaaaatc ccaggagttt tgtgtgtgga gtctggggtt ttccaacaga 240
catcattcca gcattctgag attagggnga ttggggatca ttctggagtt ggaatgttca 300
acaaaagtga tgttgttagg taaaatgtac aacttctgga tctatgcaga cattgaagggt 360
gcaatgagtc tggcttttac tctgctgttt ct 392

```

```

<210> 432
<211> 387
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(387)
<223> n = A,T,C or G

```

```

<400> 432
ggtatccta cataatcaaa tatagctgta gtacatgttt tcattggngt agattaccac 60
aaatgcaagg caacatgtgt agatctcttg tcttattctt ttgtctataa tactgtattg 120
ngtagtccaa gctctcgna gtccagccac tngnaaacat gtcctcttta gattaacctc 180
gtggacnctn ttgttgnatt gtctgaactg tagngccctg tatcttctgt ctgtctgnga 240
attctgttgc ttctggggca ttctcttng atgcagagga ccaccacaca gatgacagca 300
atctgaattg ntccaatcac agctgcgatt aagacatact gaaatcgtac aggaccggga 360
acaacgtata gaacactgga gtccttt 387

```

```

<210> 433
<211> 281
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(281)
<223> n = A,T,C or G

```

```

<400> 433
ttcaactagc anagaanact gcttcagggn gtgtaaaatg aaaggcttcc acgcagttat 60

```

148

```

ctgattaaag aacactaaga gagggacaag gctagaagcc gcaggatgtc tacactatag 120
caggcnctat ttgggttggc tggaggagct gtggaaaaca tggagagatt ggcgctggag 180
atgcgcgtgg ctattcctcn ttgntattac accagnaggg ntctctgtnt gccactgggt 240
tnnaaaaccg ntatacaata atgatagaat aggacacaca t 281

```

&lt;210&gt; 434

&lt;211&gt; 484

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 434

```

ttttaaaata agcatttagt gctcagtcct tactgagtac tctttctctc cctcctctctg 60
aatttaattc tttcaacttg caatttgcaa ggattacaca tttcactgtg atgtatatg 120
tggtgcaaaa aaaaaaaagt gtctttgttt aaaattactt gggttgtaa tccatcttgc 180
tttttcccca ttggaactag tcattaaccc atctctgaac tggtagaaaa acatctgaag 240
agctagtcta tcagcatctg acaggtgaat tggatggttc tcagaacctt ttcaccaga 300
cagcctgttt ctatcctgtt taataaatta gtttgggttc tctacatgca taacaaacc 360
tgctccaatc tgtcacataa aagtctgtga cttgaagttt agtcagcacc cccaccaaac 420
tttatttttc tatgtgtttt ttgcaacata tgagtgtttt gaaaataaag taccatgtc 480
ttta 484

```

&lt;210&gt; 435

&lt;211&gt; 424

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 435

```

gcgccgctca gagcaggtea ctttctgcct tccacgtcct ccttcaagga agcccatgt 60
gggtagcttt caatctgca ggttcttact cctctgcctc tataagctca aaccaccaa 120
cgatcgggca agtaaacccc ctccctcgcc gacttcggaa ctggcgagag ttcagcgag 180
atgggcctgt ggggaggggg caagatagat gagggggagc ggcatggtgc ggggtgacc 240
cttgagaga ggaanaaggc cacaagaggg gctgccaccg ccactaacgg agatggcct 300
ggtagagacc tttgggggtc tggaacctct ggactcccca tgctctaact cccacactct 360
gctatcagaa acttaaacctt gaggattttc tctgtttttc actcgcaata aattcagagc 420
aac 424

```

&lt;210&gt; 436

&lt;211&gt; 667

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(667)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 436

```

accttgggaa nactctcaca atataaaggg tcgtagactt tactccaat tccaaaaagg 60
tcctggccat gtaatcctga aagttttccc aaggtagcta taaaatcctt ataagggtgc 120
agcctcttct ggaattcctc tgatttcaaa gtctcactct caagttcttg aaaacgaggg 180
cagttcctga aaggcaggta tagcaactga tcttcagaaa gaggaactgt gtgcaccggg 240
atgggctgcc agagtaggat aggattccag atgctgacac cttctggggg aaacagggct 300
gccaggtttg tcatagcact catcaaagtc cggccaacgt ctgtgcttgc aatataaacc 360
tgttcatgtt tataggactc attcaagaat tttctatata tctttcttat atactctcca 420
agttcataat gctgctccat gccagctggg gtgagttggc caaatccttg tggccatgag 480
gattccttta tggggtcagt gggaagggtg tcaatgggac ttcggtctcc atgccgaac 540
accaaaagtc caaacttcaa ctcttggctc agtacacttc ggtctagcca gaaaaaagg 600
agaacaaga agccaaggct aaggcttgct gcctgccag gaggggggt gcagctctca 660

```

149

tggttgag

667

&lt;210&gt; 437

&lt;211&gt; 693

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 437

```

ctacgtctca accctcattt ttaggtaagg aatcttaagt ccaaagatat taagtgactc 60
acacagccag gtaaggaaag ctggattggc aactaggac tctaccatac cgggttttgt 120
taaagctcag gttaggaggc tgataagctt ggaaggaaact tcagacagct ttttcagatc 180
ataaaagata attcttagcc catgttcttc tccagagcag acctgaaatg acagcacagc 240
aggctactcct ctatcttcac cctcttgct tctactctct ggcagtcaga cctgtgggag 300
gccatgggag aaagcagctc tctggatgtt tgtacagatc atggactatt ctctgtggac 360
catttctcca ggttacccta ggtgtcacta ttgggggggac agccagcatc ttttagctttc 420
atttgagttt ctgtctgtct tcagtagagg aaacttttgc tcttcacact tcacatctga 480
acacctaaact gctgttgctc ctgaggtggt gaaagacaga tatagagctt acagtattta 540
tcctatttct aggcactgag ggctgtgggg taccttgttg tgccaaaaca gatcctgttt 600
taaggacatg ttgcttcaga gatgtctgta actatctggg ggctctgttg gctctttacc 660
ctgcatcatg tgctctcttg gctgaaaatg acc                                     693

```

&lt;210&gt; 438

&lt;211&gt; 360

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 438

```

ctgcttatca caatgaatgt tctcctgggc agcgttgtga tctttgccac cttcgtgact 60
ttatgcaatg catcatgcta tttcatacct aatgaggagg ttccaggaga ttcaaccagg 120
atgtttctac acctgtgggt tatgacaaag acaactgcc aagaatcttc aagaaggagg 180
actgcaagta tatctggttg agaagaagga cccaaaaaag acctgttctg tcagtgaatg 240
gataatctaa tgtgcttcta gtaggcacag ggtccagg ccaggcctca ttctcctctg 300
gcctctaata gtcaataatt gtgtagccat gcctatcagt aaaaagattt ttgagcaaac 360

```

&lt;210&gt; 439

&lt;211&gt; 431

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(431)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 439

```

gttcctnnta actcctgcc a gaaacagctc tctcaacat gagagctgca cccctcctcc 60
tggccagggc agcaagcctt agccttggct tcttgtttct gcttttttct tggctagacc 120
gaagtgtact agccaaggag ttgaagtttg tgactttggt gtttcggcat ggagaccgaa 180
gtcccattga cacttttccc actgaccca taaaggaatc ctcatggcca caaggatttg 240
gccaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaaga 300
gatatagaaa attcttgaat gagtccata aacatgaaca ggtttatatt cgaagcacag 360
acgttgaccg gactttgatg agtgctatga caaacctggc agcccgctga cgcggccgcg 420
aatttagtag t                                     431

```

&lt;210&gt; 440

&lt;211&gt; 523

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

150

&lt;400&gt; 440

```

agagataaag cttaggtcaa agttcataga gttcccatga actatatgac tggccacaca 60
ggatccttttg tatttaagga ttctgagatt ttgcttgagc aggattagat aaggctgttc 120
tttaaatgtc tgaaatggaa cagatttcaa aaaaaaaccc cacaatctag ggtgggaaca 180
aggaaggaaa gatgtgaata ggctgatggg caaaaaacca atttacccat cagttccagc 240
cttctctcaa ggagaggcaa agaaaggaga tacagtggag acatctggaa agttttctcc 300
actggaaac tgctactatc tgtttttata tttctgttaa aatatatgag gctacagaac 360
taaaaattaa aacctctttg tgtcccttgg tcctggaaca tttatgttcc ttttaaagaa 420
acaaaaatca aactttacag aaagatttga tgtatgtaat acatatagca gctcttgaag 480
tatatatatc atagcaaata agtcactctga tgagaacaag cta 523

```

&lt;210&gt; 441

&lt;211&gt; 430

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 441

```

gttcctccta actcctgcca gaaacagctc tcctcaacat gagagctgca cccctcctcc 60
tgccagggc agcaagcctt agccttggct tcttgtttct gcttttttcc tggctagacc 120
gaagtgtact agccaaggag ttgaagttag tgactttggg gtttcggcat ggagaccgaa 180
gtcccattga cacctttccc actgacccca taaaggaatc ctcatggcca caaggatttg 240
gccaaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
gatatagaaa attccttgaat gagtccata aacatgaaca ggtttatatt cgaagcacag 360
acgttgaccg gactttgatg agtgctatga caaacctggc agcccgtcga cgcggccgcg 420
aatttagtag 430

```

&lt;210&gt; 442

&lt;211&gt; 362

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 442

```

ctaaggaatt agtagtggtc ccatcacttg tttggagtgt gctattctaa aagattttga 60
tttcctggaa tgacaattat attttaactt tggtagggga aagagttata ggaccacagt 120
cttcacttct gatacttgta aattaatott ttattgcact tgttttgacc attaatgtat 180
atgttttagaa atgggtcattt tacggaaaaa ttagaaaaat tctgataata gtgcagaata 240
aatgaattaa tgttttactt aatttatatt gaactgtcaa tgacaaataa aaattctttt 300
tgattatatt ttgttttcat ttaccagaat aaaaactaag aattaaaagt ttgattacag 360
tc 362

```

&lt;210&gt; 443

&lt;211&gt; 624

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(624)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 443

```

tttttttttt gcaacacaat atacatcaca gtgaaatgtg taatccttgc aaattgcaag 60
ttgaaagaat taaattcaga ggaggggaga gaaagagtag tcagtaggga ctgagcacta 120
aatgcttatt ttaaaagaaa tgtaaagagc agaaagcaat tcaggctacc ctgccttttg 180
tgctggctag tactccggtc ggtgtcagca gcacgtggca ttgaacattg caatgtggag 240
cccaaaccac agaaaatggg gtgaaattgg ccaactttct attaaacttg cttcctgttt 300
tataaaatat tgtgaataat atcacctact tcaaagggca gttatgaggc ttaaatgaac 360

```

151

```

taacgcctac aaaacactta aacatagata acatagggtgc aagtactatg tatctgggtac 420
atggtaaaca tccttattat taaagtcaac gctaaaatga atgtgtgtgc atatgctaata 480
agtacagaga gagggcactt aaaccaacta agggcctgga ggaaggttt cctggaaaga 540
ngatgcttgt gctgggtcca aatcttggtc tactatgacc ttggccaaat tatttaaact 600
ttgtccctat ctgctaaaca gatc 624

```

```

<210> 444
<211> 425
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(425)
<223> n = A,T,C or G

```

```

<400> 444
gcacatcatt nntcttgcatt tctttgagaa taagaagatc agtaaatagt tcagaagtgg 60
gaagctttgt ccaggcctgt gtgtgaaccc aatgttttgc ttagaaatag aacaagtaag 120
ttcattgcta tagcataaca caaaatttgc ataagtgggtg gtcagcaaat ccttgaatgc 180
tgcttaatgt gagagggttg taaaatcctt tgtgcaacac tctaactccc tgaatgtttt 240
gctgtgctgg gacctgtgca tgccagacaa ggccaagctg gctgaaagag caaccagcca 300
cctctgcaat ctgccacctc ctgctggcag gatttgtttt tgcacctgtg gaagagccaa 360
ggaggcacca gggcataagt gagtagactt atggtcgacg cggccgcgaa ttagtagta 420
gtaga 425

```

```

<210> 445
<211> 414
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(414)
<223> n = A,T,C or G

```

```

<400> 445
catgttttatg nttttggatt actttgggca cctagtgttt ctaaatogtc tatcattcctt 60
ttctgtttttt caaaagcaga gatggccaga gtctcaacaa actgtatcctt caagtctttg 120
tgaaattcctt tgcattgtggc agattattgg atgtagtctt cttaactag catataaatc 180
tggtgtgtttt cagataaatg aacagcaaaa tgtgggtgaa ttaccatttg gaacattgtg 240
aatgaaaaat tgtgtctcta gattatgtaa caaataacta tttcctaacc attgatcttt 300
ggatttttat aatcctactc acaaatgact aggtttotcc tcttgtattt tgaagcagtg 360
tggtgtgctgg attgataaaa aaaaaaaag tcgacgcggc cgcgaattta gtag 414

```

```

<210> 446
<211> 631
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(631)
<223> n = A,T,C or G

```

```

<400> 446
acaaattaga anaaagtgcc agagaacacc acataccttg tccggaacat tacaatggct 60
tctgcatgca tgggaagtgt gagcattcta tcaatatgca ggagccatct tgcagggtgtg 120

```



152

```

atgctgggta tactggacaa cactgtgaaa aaaaggacta cagtgttcta tacgttggtc 180
ccggtcctgt acgatttcoag tatgtcttaa tcgcagctgt gattggaaca attcagattg 240
ctgtcatctg tgtgggtggc ctctgcatca caagggccaa actttaggta atagcattgg 300
actgagattt gtaaaactttc caaccttcca ggaaatgcc cagaagcaac agaattcaca 360
gacagaagca aaatacaggg cactacagtt cagacaatac aacaagagcg tccacgaggt 420
taatctaaag ggagcatggt tcacagtggc tggactaccg agagcttgga ctacacaata 480
cagtattata gacaaaagaa taagacaaga gatctacaca tgttgccttg catttggtgt 540
aatctacacc aatgaaaaca tgtactacag ctatatattga ttatgtatgg atatatattga 600
aatagtatac attgtcttga tgttttttct g 631

```

&lt;210&gt; 447

&lt;211&gt; 585

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(585)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 447

```

ccttgggaaa antntcacia tataaagggt cgtagacttt actccaaatt ccaaaaagggt 60
cctggccatg taatcctgaa agttttccca aggtagctat aaaatcctta taagggtgca 120
gcctcttctg gaattcctct gatttcaaag tctcactctc aagttcttga aaacgagggc 180
agttcctgaa aggcaggtat agcaactgat cttcagaaag aggaactgtg tgcaccggga 240
tgggctgcca gagtaggata ggattccaga tgctgacacc ttctggggga aacagggtctg 300
ccaggtttgt catagcactc atcaaagtc ggtcaacgtc tgtgcttoga atataaacct 360
gttcatgttt ataggactca ttcaagaatt ttctatatct ctttcttata tactctccaa 420
gttcataatg ctgctccatg cccagctggg tgagttggcc aaatccttgt ggccatgagg 480
attcctttat ggggtcagtg ggaaagggtg caatgggact tcggtctcca tgccgaaaca 540
ccaaagtcac aaacttcaac tccttggtca gtacacttcg gtcta 585

```

&lt;210&gt; 448

&lt;211&gt; 93

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(93)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 448

```

tgctcgtggg tcattctgan nnccgaactg acctgcccag ccctgccgan gggccnccat 60
ggctccctag tgccctggag agganggggc tag 93

```

&lt;210&gt; 449

&lt;211&gt; 706

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(706)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 449

```

ccaagttcat gctntgtgct ggacgctgga cagggggcaa aagcnnttgc tcgtgggtca 60

```

153

```

ttctgancac cgaactgacc atgccagccc tgcgatggt cctccatggc tccctagtgc 120
cctggagagg aggtgtctag tcagagagta gtcctggaag gtggcctctg ngaggagcca 180
cggggacagc atcctgcaga tggtcgggcg cgtccattc gccattcagg ctgcgcaact 240
gttgggaagg gcgatcggtg cgggcctctt cgtattacg ccagctggcg aaagggggat 300
gtgctgcaag gcgattaagt tgggtaacgc cagggttttc ccagtcncga cgttgtaaaa 360
cgacggccag tgaattgaat ttaggtgacn ctatagaaga gctatgacgt cgcattgcacg 420
cgtacgtaag cttggatcct cttagcgggc cgcctactac tactaaattc gcggcgcgct 480
cgacgtggga tccnactga gagagtggag agtgacatgt gctggacnct gtccatgaag 540
cactgagcag aagctggagg cacaacgcnc cagacactca cagctactca ggaggctgag 600
aacaggttga acctgggagg tggaggttgc aatgagctga gatcaggccn ctgcncccca 660
gcatggatga cagagtgaag ctccatctta aaaaaaaaaa aaaaaa 706

```

&lt;210&gt; 450

&lt;211&gt; 493

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 450

```

gagacggagt gtcactctgt tgcccaggct ggagtgcagc aagacactgt ctaagaaaaa 60
acagttttta aaggtaaaac aacataaaaa gaaatatcct atagtggaaa taagagagtc 120
aaatgaggct gagaacttta caaagggatc ttacagacat gtcgccaata tcaactgcatg 180
agcctaagta taagaacaac ctttggggag aaaccatcat ttgacagtga ggtacaattc 240
caagtcagggt agtgaatgg gtggaattaa actcaaatta atcctgccag ctgaaacgca 300
agagacactg tcagagagtt aaaaagttag ttctatccat gaggtgattc cacagtcttc 360
tcaagtcaac acatctgtga actcacagac caagttctta aaccactgtt caaactctgc 420
tacacatcag aatcacctgg agagctttac aaactcccat tgccgagggg cgacgcgggc 480
gcgaatttag tag 493

```

&lt;210&gt; 451

&lt;211&gt; 501

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(501)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 451

```

gggcgcgtcc cattcgccat tcaggctgcg caactgttgg gaagggcgat cgggtgcgggc 60
ctcttcgcta ttacgccagc tggcgaaagg ggcatgtgct gcaaggcgat taagttgggt 120
aacgccaggg ttttccagc cncgacgttg taaaacgacg gccagtgaat tgaatttagg 180
tgacnctata gaagagctat gacgtcgcat gcacgcgtac gtaagcttgg atcctctaga 240
gcggccgcct actactacta aattcgcgcg cgcgtcgacg tgggatccnc actgagagag 300
tgagagtgga catgtgctgg acnctgtcca tgaagcactg agcagaagct ggaggcacia 360
cgcnccagac actcacagct actcaggagg ctgagaacag gttgaacctg ggagggtggag 420
gttgcaatga gctgagatca ggcnctgcn ccccgacatg gatgacagag tgaaactcca 480
tcttaaaaaa aaaaaaaaaa a 501

```

&lt;210&gt; 452

&lt;211&gt; 51

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(51)

&lt;223&gt; n = A,T,C or G

154

```

<400> 452
agacggtttc accnttacaa cnccttttag gatgggnntt ggggagcaag c      51

<210> 453
<211> 317
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(317)
<223> n = A,T,C or G

<400> 453
tacatcttgc tttttcccca ttggaactag tcattaaccc atctctgaac tggtagaaaa 60
acatctgaag agctagtcta tcagcatctg gcaagtgaat tggatgggtc tcagaacccat 120
ttcaccana cagcctgttt ctatcctgtt taataaatta gtttgggttc tctacatgca 180
taacaaaccc tgctccaatc tgtcacataa aagtctgtga cttgaagttt antcagcacc 240
cccacaaac tttatttttc tatgtgtttt ttgcaacata tgagtgtttt gaaaataagg 300
taccatgtc tttatta                                     317

<210> 454
<211> 231
<212> DNA
<213> Homo sapiens

<400> 454
ttcgaggtag aatcaactct cagagtgtag tttccttcta tagatgagtc agcattaata 60
taagccacgc cagctctctg aaggagtctt gaattctcct ctgctcactc agtagaacca 120
agaagaccaa attcttctgc atcccagctt gcaaacaaaa ttgttcttct aggtctccac 180
ccttctttt tcagtgttcc aaagctctc acaatttcat gaacaacagc t      231

<210> 455
<211> 231
<212> DNA
<213> Homo sapiens

<400> 455
taccaaagag ggcataataa tcagtctcac agtaggggtc accatcctcc aagtgaaaaa 60
cattgttccg aatgggcttt ccacaggcta cacacacaaa acaggaaaca tgccaagttt 120
gtttcaacgc attgatgact tctccaagga tcttcctttg gcatcgacca cattcagggg 180
caaagaattt ctcatagcac agctcacaat acagggtcc tttctcctct a      231

<210> 456
<211> 231
<212> DNA
<213> Homo sapiens

<400> 456
ttggcaggta cccttacaaa gaagacacca taccttatgc gttattaggt ggaataatca 60
ttccattcag tattatcggtt attattcttg gagaaaccct gtctgtttac tgtaaccttt 120
tgactcaaaa ttcctttatc aggaataact acatagccac tatttacaaa gccattggaa 180
cctttttatt tgggtcagct gctagtcagt ccctgactga cattgccaag t      231

<210> 457
<211> 231
<212> DNA

```

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(231)

<223> n = A,T,C or G

<400> 457

```
cgaggtaccc aggggtctga aaatctctnn tttantagtc gatagcaaaa ttgttcatca 60
gcattcctta atatgatctt gctataatta gatTTTTtctc cattagagtt catacagttt 120
tatttgattt tattagcaat ctctttcaga agacccttga gatcattaag ctttgtatcc 180
agttgtctaa atcgatgcct catttcctct gaggtgtcgc tggcttttgt g 231
```

<210> 458

<211> 231

<212> DNA

<213> Homo sapiens

<400> 458

```
aggtctggtt cccccactt ccactcccct ctactctctc taggactggg ctgggccaaag 60
agaagagggg tggttaggga agccgttgag acctgaagcc ccacctcta ccttccttca 120
acaccctaac cttgggtaac agcatttga attatcattt gggatgagta gaatttccaa 180
ggtcctgggt taggcatttt ggggggccag accccaggag aagaagattc t 231
```

<210> 459

<211> 231

<212> DNA

<213> Homo sapiens

<400> 459

```
ggtaccgagg ctgctgaca cagagaaacc ccaacgcgag gaaaggaatg gccagccaca 60
ccttcgcgaa acctgtggtg gccaccagt cctaacggga caggacagag agacagagca 120
gccctgcact gttttccctc caccacagcc atcctgtccc tcattggctc tgtgctttcc 180
actatacaca gtcaccgtcc caatgagaaa caagaaggag caccctccac a 231
```

<210> 460

<211> 231

<212> DNA

<213> Homo sapiens

<400> 460

```
gcaggtataa catgctgcaa caacagatgt gactaggaac ggccggtgac atggggaggg 60
cctatcaccc tattcttggg ggctgcttct tcacagtgat catgaagcct agcagcaa 120
cccacctccc cacacgcaca cggccagcct ggagcccaca gaagggtcct cctgcagcca 180
gtggagcttg gtccagcctc cagtccaccc ctaccaggct taaggataga a 231
```

<210> 461

<211> 231

<212> DNA

<213> Homo sapiens

<400> 461

```
cgaggtttga gaagctctaa tgtgcagggg agccgagaag caggcggcct agggagggtc 60
gcgtgtgctc cagaagagtgt tgtgcatgcc agaggggaaa caggcgccctg tgtgtcctgg 120
gtggggttca gtgaggagtgt ggaaattggt tcagcagaac caagccgttg ggtgaataag 180
agggggattc catggcactg atagagccct atagtttcag agctgggaat t 231
```

<210> 462

156

<211> 231  
<212> DNA  
<213> Homo sapiens

<400> 462  
aggtaccctc attgtagcca tgggaaaatt gatgttcagt ggggatcagt gaattaaatg 60  
gggtcatgca agtataaaaa ttaaaaaaaa aagacttcat gcccaatctc atatgatgtg 120  
gaagaactgt tagagagacc aacagggtag tgggttagag atttccagag tcttacattt 180  
tctagaggag gtattttaatt tcttctcact catccagtgt tgtatttagg a 231

<210> 463  
<211> 231  
<212> DNA  
<213> Homo sapiens

<400> 463  
tactccagcc tggtgacaga gcgagaccct atcaccgccc cccacccccc caaaaaaaaa 60  
actgagtaga caggtgtcct cttggcatgg taagtcttaa gtcccctccc agatctgtga 120  
catttgacag gtgtcttttc ctctggacct cgggtgcccc atctgagtga gaaaaggcag 180  
tggggagggtg gatcttccag tcgaagcggt atagaagccc gtgtgaaaag c 231

<210> 464  
<211> 231  
<212> DNA  
<213> Homo sapiens

<400> 464  
gtactctaag attttatcta agttgccttt tctgggtggg aaagtttaac cttagtgaact 60  
aaggacatca catatgaaga atgtttaagt tggagggtggc aacgtgaatt gcaaacaggg 120  
cctgtctcag tgaactgtgtg cctgtagtcc cagctactcg ggagtctgtg tgaggccagg 180  
ggtgccagcg caccagctag atgctctgta acttctaggg cccattttcc c 231

<210> 465  
<211> 231  
<212> DNA  
<213> Homo sapiens

<400> 465  
catgttggtg tagctgtggt aatgctggct gcatctcaga cagggttaac ttcagctcct 60  
gtggcaaatt agcaacaaat tctgacatca tatttatggt ttctgtatct ttgttgatga 120  
aggatggcac aatttttggct tgtgttcata atatactcag attagtccag ctccatcaga 180  
taaactggag acatgcagga cattagggtg gtgtttagtc tctggtaatg a 231

<210> 466  
<211> 231  
<212> DNA  
<213> Homo sapiens

<400> 466  
caggtaacct tttccattgg ataactgtgt agcaagcatg ctctccgggg tttttttaat 60  
ggccttcgaa cagaacttgc cacataccca ggtataatag tttctaactt ttgccaggga 120  
cctgtgcaat caaatattgt ggagaattcc ctgactggag aagtcacaaa gactataggg 180  
aataatggag accagtccca caagatgaca accagtctgt gtgtgagggt g 231

<210> 467  
<211> 311  
<212> DNA  
<213> Homo sapiens

&lt;400&gt; 467

```

gtacaccctg gcacagtcca atctgaactg gttcggcact catctttcat gagatggatg 60
tggtggcctt tctccttttt catcaagact cctcagcagg gagcccagac cagcctgcac 120
tgtgccttaa cagaaggctt tgagattcta agtgggaatc atttcagtga ctgtcatgtg 180
gcatgggtct ctgcccaagc tcgtaatgag actatagcaa ggcggtgtg ggacgtcagt 240
tgtgacctgc tgggcctccc aatagactaa caggcagtgc cagttggacc caagagaaga 300
ctgcagcaga c                                     311

```

&lt;210&gt; 468

&lt;211&gt; 3112

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 468

```

cattgtgttg ggagaaaaac agaggggaga tttgtgtggc tgcagccgag ggagaccagg 60
aagatctgca tgggtgggaag gacctgatga tacagagttt gataggagac aattaaaggc 120
tggaaggcac tggatgcctg atgatgaagt ggactttcaa actggggcac tactgaaacg 180
atgggatggc cagagacaca ggagatgagt tggagcaagc tcaataacaa agtgggtcaa 240
cgaggacttg gaattgcatg gagctggagc tgaagttag cccaattgtt tactagttag 300
gtgaatgttg atgattggat gatcatttct catctctgag cctcaggttc cccatccata 360
aaatgggata cacagtatga tctataaagt gggatatagt atgatctact tccctgggtt 420
atgtgaagga tgaattgaga taatttatit cagggtgccta gaacaatgcc cagattagta 480
catttgggtg aactgagaaa tggcataaca ccaaatttaa tatatgtcag atgttactat 540
gattatcatt caatctcata gttttgtcat ggcccaattt atcctcactt gtgcctcaac 600
aaattgaact gtttaacaaag gaatctctgg tctgggttaa tggctgagca ccactgagca 660
tttccattcc agttggcctt ttgggtttgc tagctgcac actagtcac ttaaataaat 720
gaagttttaa catttctcca gtgatttttt tatctcacct ttgaagatac tatgttatgt 780
gattaaataa agaacttgag aagaacaggt ttcattaaac ataaaatcaa tgtagacgca 840
aattttctgg atgggcaata cttatgttca caggaaatgc tttaaaatat gcagaagata 900
attaaatggc aatggacaaa gtgaaaaact tagacttttt tttttttttt ggaagtatct 960
ggatgttcct tagtcactta aaggagaact gaaaaatagc agtgagttcc acataatcca 1020
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&lt;210&gt; 469

&lt;211&gt; 2229

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 469

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&lt;210&gt; 470

&lt;211&gt; 2426

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 470

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&lt;210&gt; 471

&lt;211&gt; 812

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 471

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160

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&lt;210&gt; 472

&lt;211&gt; 515

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(515)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 472

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&lt;210&gt; 473

&lt;211&gt; 5829

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 473

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162

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aaaaaaaaa 5829

```

&lt;210&gt; 474

&lt;211&gt; 1594

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 474

```

atttatggat cattaatgcc tcttttagtag ttttagagaaa acgtcaaaaag aaatggcccc 60
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aaaatataaa tatatagaca tctcagataa tatatttgaa atagcaaatt cctgttagaa 180
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gttttcagaa ttattgtatg cagtcagtat gagaatgcaa tttaagtttc cttgatgctt 360
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gaagggaaga ggctggggc tggagtattc gctt 1594

```

&lt;210&gt; 475

&lt;211&gt; 2414

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; unsure

&lt;222&gt; (33)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 475

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aaaaaaaaaa aaaa 2414

```

&lt;210&gt; 476

&lt;211&gt; 3434

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 476

```

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aaaaaaaaaa aaaa 3434

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&lt;210&gt; 477

&lt;211&gt; 140

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

165

&lt;400&gt; 477

```

Met Asp Gly His Thr Asp Ile Trp Arg Asn His Met Asp Thr Pro Pro
                    5                               10                15
His Tyr His Arg Asp Thr Asp Thr Arg Arg His His His Met Asp Thr
                20                               25                30
Leu Ser His Tyr His Arg Asp Thr Arg His His Thr Val Thr Trp Thr
                35                               40                45
His His His Thr His Glu His Thr Asp Thr Leu Pro Tyr Gly His Trp
                50                               55                60
His Thr His Cys His Thr Val Thr Trp Thr His Leu His Thr Ile Thr
                65                               70                75                80
Pro Pro His Thr Leu Pro Val Asp Thr Arg Thr His Arg His Cys His
                85                               90                95
Thr Asp Thr Gln Asn Thr Val Thr Arg Arg His His His Ala Asp Thr
                100                               105                110
Pro Pro Leu Trp Cys Arg Leu Asn Tyr Pro Ala Gly Gly Thr Ala Val
                115                               120                125
Ala Tyr Ser Cys Leu Ser Asp Trp Leu Ser Pro Gln
                130                               135                140

```

&lt;210&gt; 478

&lt;211&gt; 143

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 478

```

Met Tyr Arg His Thr Glu Thr Leu Pro His Gly Asp Thr Val Thr Gln
                    5                               10                15
Ser His Gly His Thr Gly Ile Val Thr Trp Thr Asp Thr Gln Thr Tyr
                20                               25                30
Gly Glu Ile Thr Trp Thr His His Thr Ile Thr Gly Thr Gln Thr
                35                               40                45
His Gly Asp Ile Thr Thr Trp Thr His Cys His Thr Thr Thr Gly Thr
                50                               55                60
Arg Asp Ile Thr Leu Ser His Gly His Thr Ile Thr His Met Asn Thr
                65                               70                75                80
Pro Thr His Cys His Met Asp Thr Gly Thr His Thr Ala Thr Leu Ser
                85                               90                95
His Gly His Thr Ser Thr Pro Ser His His Thr His Cys Leu Trp
                100                               105                110
Thr Gln Gly His Thr Asp Thr Val Thr Gln Ile His Lys Thr Leu Ser
                115                               120                125
His Gly Asp Ile Thr Met Gln Ile His His His Ser Gly Ala Val
                130                               135                140

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&lt;210&gt; 479

&lt;211&gt; 222

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 479

```

Met Tyr Arg His Thr Glu Thr Leu Pro His Gly Asp Thr Val Thr Gln
                    5                               10                15
Ser His Glu His Thr Gly Ile Val Thr Trp Thr Asp Thr Gln Thr Tyr
                20                               25                30

```

166

Gly Glu Ile Thr Leu Thr His His His Thr Ile Thr Gly Thr Gln Thr  
           35                          40                          45  
 His Gly Asp Ile Thr Thr Trp Thr His Cys His Thr Thr Thr Gly Thr  
           50                          55                          60  
 Arg Asp Ile Thr Leu Ser His Gly His Thr Ile Thr His Met Asn Thr  
           65                          70                          75                          80  
 Pro Thr His Cys His Met Asp Thr Ala Thr His Thr Ala Thr Leu Ser  
                           85                          90                          95  
 His Gly His Thr Ser Ile Pro Ser His His His Thr His Cys His Val  
                           100                          105                          110  
 Asp Thr Arg Thr His Arg His Cys His Thr Asp Thr Gln Asn Thr Val  
                           115                          120                          125  
 Thr Arg Arg His His His Ala Asp Thr Pro Pro His Gly His Ser Thr  
                           130                          135                          140  
 Arg His Ser Ala Thr Gln Ile His His His Thr Glu Met Arg Thr His  
           145                          150                          155                          160  
 Cys His Thr Asp Thr Thr Thr Ser Leu Pro His Phe His Val Ser Ala  
                           165                          170                          175  
 Gly Gly Val Gly Pro Thr Thr Leu Gly Ser Asn Arg Glu Ile Thr Trp  
                           180                          185                          190  
 Thr Tyr Ser Glu Gly Lys Ile Phe Phe Tyr Phe Leu Gly Asn Gln Ala  
                           195                          200                          205  
 Arg Leu Cys Leu Lys Lys Arg Lys Lys Lys Gln Tyr Thr Val  
           210                          215                          220

&lt;210&gt; 480

&lt;211&gt; 144

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 480

Met Glu Pro Tyr Arg Gly Asn Glu Gln Pro Ser Gln Glu Gln Gly Val  
                           5                          10                          15  
 Cys Cys Leu Trp Gly Leu Gln Ser Leu Pro Gln Gly Ser Tyr Val Thr  
                           20                          25                          30  
 Val Gly Phe Leu Val Val Lys Arg Gln Thr Ile Gly Arg Leu Glu Arg  
                           35                          40                          45  
 Asp Phe Met Phe Lys Cys Arg Lys Gln Pro Gly Leu Pro Pro Ser Gly  
           50                          55                          60  
 Leu Cys Leu Leu Trp Pro Trp Pro Asn Leu Glu Phe Gly Arg Arg Gln  
           65                          70                          75                          80  
 Asp Arg Leu Thr Trp Ser Ser Val Ser Val Ala Gly Val Cys Ala Cys  
                           85                          90                          95  
 Arg Ala Arg Pro Gly Trp Leu Gly Glu Gln Pro Ala Thr Ser Ala Gly  
                           100                          105                          110  
 Val Arg Leu Glu Gln Val Glu Gln Pro Pro Ala His Pro Leu Gln Glu  
                           115                          120                          125  
 Ala Gly Val Ala Arg Phe Pro Arg Pro Glu Trp Val Pro Pro Asn Gly  
           130                          135                          140

&lt;210&gt; 481

&lt;211&gt; 167

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 481

167

[illegible]

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<210> 482
<211> 143
<212> PRT
<213> Homo sapiens
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<400> 482																
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Pro	Cys	Leu	Trp	Gly	Ser	Ser	Pro	Cys	Leu	Arg	Cys	His	Met	Ala	Leu	
			20					25					30			
Arg	Ala	Ser	Trp	Leu	Pro	Gly	Gly	Gly	Pro	Gln	Ala	Ile	Leu	Gly	Arg	
			35				40					45				
Thr	Leu	Cys	Ser	Ser	Ala	Glu	Ser	Ser	Gln	Asp	Cys	His	Pro	Gly	Gly	
	50					55					60					
Pro	Ser	Ile	Ala	Leu	Ala	Lys	Pro	Cys	Arg	Gly	Val	Trp	Leu	Leu	Phe	
	65				70					75					80	
Glu	Pro	Ala	Trp	Pro	Pro	Trp	His	Ala	Arg	Ala	Pro	Gly	Ala	Gly	Thr	
				85					90					95		
Leu	Leu	Arg	Val	Cys	Leu	Ser	Cys	Leu	Gly	Cys	His	Leu	Cys	Gly	Gly	
			100					105				110				
Ala	Ser	Gly	Gly	Gly	Gly	Pro	Ala	Thr	Asn	Leu	Thr	Gln	Ser	Arg	Lys	
		115				120						125				
Trp	Met	Ala	Met	Phe	Pro	Gln	Pro	Glu	Trp	Leu	Pro	Pro	Asp	Gly		
	130					135					140					

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<210> 483
<211> 143
<212> PRT
<213> Homo sapiens
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<400> 483
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Cys Cys Leu Trp Gly Ser Ser Pro Cys Leu Gly Ser Tyr Gly Thr Ala

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168

20 25 30  
 Gly Phe Leu Val Ala Lys Arg Arg Thr Thr Gly Leu Leu Glu Glu Asp  
 35 40 45  
 Phe Thr Phe Lys Cys Arg Lys Gln Pro Lys Leu Pro Ser Met Arg Leu  
 50 55 60  
 Ser Leu Leu Trp Pro Trp Arg Asp Leu Lys Phe Val Pro Arg Gln Asp  
 65 70 75 80  
 Lys Leu Thr Arg Ser Ser Val Ser Val Ala Gly Ala Tyr Ala Cys Arg  
 85 90 95  
 Ala Gly Pro Gly Trp Leu Lys Glu Gln Pro Ala Thr Ser Ala Arg Val  
 100 105 110  
 Arg Leu Val Gln Ala Glu His Pro Pro His Pro Leu Glu Glu Val  
 115 120 125  
 Gly Met Ala Arg Phe Pro Gln Pro Glu Cys Leu Pro Pro Tyr Cys  
 130 135 140

<210> 484  
 <211> 30  
 <212> PRT  
 <213> Homo Sapien

<400> 484  
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 1 5 10 15  
 Ala Ile Pro Ile Gly Gln Ala Met Ala Ile Ala Gly Gln Ile  
 20 25 30

<210> 485  
 <211> 31  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 485  
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31

<210> 486  
 <211> 27  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 486  
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27

<210> 487  
 <211> 36  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 487

169

cccgaaattct tagctgccca tccgaacgcc ttcac

36

<210> 488  
 <211> 33  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 488  
 gggaagcttc ttccccgggt gcaccagctg tgc

33

<210> 489  
 <211> 19  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 489  
 Met Asp Arg Leu Val Gln Arg Phe Gly Thr Arg Ala Val Tyr Leu Ala  
 1 5 10 15  
 Ser Val Ala

<210> 490  
 <211> 20  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 490  
 Tyr Leu Ala Ser Val Ala Ala Phe Pro Val Ala Ala Gly Ala Thr Cys  
 1 5 10 15  
 Leu Ser His Ser  
 20

<210> 491  
 <211> 20  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 491  
 Thr Cys Leu Ser His Ser Val Ala Val Thr Ala Ser Ala Ala Leu  
 1 5 10 15  
 Thr Gly Phe Thr  
 20

<210> 492  
 <211> 20  
 <212> PRT

170

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 492

Ala	Leu	Thr	Gly	Phe	Thr	Phe	Ser	Ala	Leu	Gln	Ile	Leu	Pro	Tyr	Thr
1				5					10					15	
Leu	Ala	Ser	Leu												
			20												

&lt;210&gt; 493

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 493

Tyr	Thr	Leu	Ala	Ser	Leu	Tyr	His	Arg	Glu	Lys	Gln	Val	Phe	Leu	Pro
1				5					10					15	
Lys	Tyr	Arg	Gly												
			20												

&lt;210&gt; 494

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 494

Leu	Pro	Lys	Tyr	Arg	Gly	Asp	Thr	Gly	Gly	Ala	Ser	Ser	Glu	Asp	Ser
1				5					10					15	
Leu	Met	Ile	Ser												
			20												

&lt;210&gt; 495

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 495

Asp	Ser	Leu	Met	Thr	Ser	Phe	Leu	Pro	Gly	Pro	Lys	Pro	Gly	Ala	Pro
1				5					10					15	
Phe	Pro	Asn	Gly												
			20												

&lt;210&gt; 496

&lt;211&gt; 21

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

171

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 496

Ala	Pro	Phe	Pro	Asn	Gly	His	Val	Gly	Ala	Gly	Gly	Ser	Gly	Leu	Leu
1				5				10						15	
Pro	Pro	Pro	Pro	Ala											
				20											

&lt;210&gt; 497

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 497

Leu	Leu	Pro	Pro	Pro	Pro	Ala	Leu	Cys	Gly	Ala	Ser	Ala	Cys	Asp	Val
1				5				10						15	
Ser	Val	Arg	Val												
			20												

&lt;210&gt; 498

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 498

Asp	Val	Ser	Val	Arg	Val	Val	Val	Gly	Glu	Pro	Thr	Glu	Ala	Arg	Val
1				5				10						15	
Val	Pro	Gly	Arg												
			20												

&lt;210&gt; 499

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 499

Arg	Val	Val	Pro	Gly	Arg	Gly	Ile	Cys	Leu	Asp	Leu	Ala	Ile	Leu	Asp
1				5				10						15	
Ser	Ala	Phe	Leu												
			20												

&lt;210&gt; 500

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

172

&lt;223&gt; Made in a lab

&lt;400&gt; 500

Leu Asp Ser Ala Phe Leu Leu Ser Gln Val Ala Pro Ser Leu Phe Met  
 1 5 10 15  
 Gly Ser Ile Val  
 20

&lt;210&gt; 501

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 501

Phe Met Gly Ser Ile Val Gln Leu Ser Gln Ser Val Thr Ala Tyr Met  
 1 5 10 15  
 Val Ser Ala Ala  
 20

&lt;210&gt; 502

&lt;211&gt; 414

&lt;212&gt; DNA

&lt;213&gt; Homo Sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(414)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 502

caccatggag	acaggcctgc	gctggctttt	cctggctcgt	gtgetcaaag	gtgtccaatg	60
tcagtcggtg	gaggagtcog	ggggtcgcct	ggtcacgcct	gggacacctt	tgacantcac	120
ctgtagagtt	tttggaatng	acctcagtag	caatgcaatg	agctgggtcc	gccaggctcc	180
aggggaaggg	ctggaatgga	tcggagccat	tgataattgt	ccacantacg	cgacctgggc	240
gaaaggccga	ttnatnattt	ccaaaacctn	gaccacggtg	gatttgaaaa	tgaccagtcc	300
gacaaccgag	gacacggcca	cctatTTTTTg	tggcagaatg	aatactggta	atagtgggtg	360
gaagaatatt	tggggcccag	gcaccctggt	caccgtntcc	tcagggaac	ctaa	414

&lt;210&gt; 503

&lt;211&gt; 379

&lt;212&gt; DNA

&lt;213&gt; Homo Sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(379)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 503

atncgatggt	gcttgggtcaa	aggtgtccag	tgctcagtcgg	tggaggagtc	cggggggtcgc	60
ctggtcacgc	ctgggacacc	cctgacactc	acctgcaccg	tntctggatt	ngacatcagt	120
agctatggag	tgagctgggt	ccgccaggct	ccagggaagg	ggctggnata	catcggtatca	180
ttagtagtag	tggtacattt	tacgcgagct	gggcgaaagg	ccgattcacc	atttccaaaa	240
cctngaccac	ggtggatttg	aaaatcacca	gtttgacaac	cgaggacacg	gccacctatt	300
tntgtgccag	aggggggttt	aattataaag	acatttgggg	cccaggcacc	ctggtcaccg	360

tntccttagg gcaacctaa

379

<210> 504  
 <211> 19  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 504  
 Gly Phe Thr Asn Tyr Thr Asp Phe Glu Asp Ser Pro Tyr Phe Lys Glu  
 1 5 10 15  
 Asn Ser Ala

<210> 505  
 <211> 20  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 505  
 Lys Glu Asn Ser Ala Phe Pro Pro Phe Cys Cys Asn Asp Asn Val Thr  
 1 5 10 15  
 Asn Thr Ala Asn  
 20

<210> 506  
 <211> 407  
 <212> DNA  
 <213> Homo Sapien

<400> 506  
 atggagacag gcctgcgctg gcttctcctg gtcgctgcgc tcaaagggtgt ccagtgtcag 60  
 tcgctggagg agtccggggg tcgcctggtc acgcctggga caccctgac actcacctgc 120  
 accgtctctg gattctccct cagtagcaat gcaatgatct gggcccgcca ggctccaggg 180  
 aaggggctgg aatacatcgg atacattagt tatggtggta gcgcatacta cgcgagctgg 240  
 gtgaaaggcc gattcaccat ctccaaaacc tcgaccacgg tggatctgag aatgaccagt 300  
 ctgacaaccg aggacacggc cacctatttc tgtgccagaa atagtgattt tagtggatatg 360  
 ttgtggggcc caggcaccct ggtcaccgtc tcctcagggc aacctaa 407

<210> 507  
 <211> 422  
 <212> DNA  
 <213> Homo Sapien

<400> 507  
 atggagacag gcctgcgctg gcttctcctg gtcgctgtgc tcaaagggtgt ccagtgtcag 60  
 tcggtggagg agtccggggg tcgcctggtc acgcctggga caccctgac actcacctgt 120  
 acagtctctg gattctccct cagcaactac gacctgaact gggcccgcca ggctccaggg 180  
 aaggggctgg aatggatcgg gatcattaat tatgttggtg ggacggacta cgcgaactgg 240  
 gcaaaaggcc gggtcaccat ctccaaaacc tcgaccacgg tggatctcaa gatcgccagt 300  
 ccgacaaccg aggacacggc cacctatttc tgtgccagag ggtggaagtg cgatgagtct 360  
 ggtccgtgct tgcgcattct gggcccaggc accctggtca ccgtctcctt agggcaacct 420

174

aa

422

<210> 508  
 <211> 411  
 <212> DNA  
 <213> Homo Sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(411)  
 <223> n=A,T,C or G

<400> 508  
 atggagacag gcctcgctgg cttctcctgg tcgctgtgct caaagggtgc cagtgtcagt 60  
 cgggtggagga gtccgggggt cgcttggtca cgctgggac acccctgaca ctcacctgca 120  
 cagtctctgg aatcgacctc agtagctact gcatgagctg ggtccgccag gctccaggga 180  
 aggggctgga atggatcgga atcattggtg ctctgggtga cacatactac gcgagggtggg 240  
 cgaaaggccg attcaccatc tccaaaacct cgaccacggt gcatntgaaa atcnccagtc 300  
 cgacaaccga ggacacggcc acctatttct gtgccagaga tcttcgggat ggtagtagta 360  
 ctggttatta taaaatctgg ggcccaggca cctgggtcac cgtctccttg g 411

<210> 509  
 <211> 15  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 509  
 Leu Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser  
 1 5 10 15

<210> 510  
 <211> 15  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 510  
 Pro Glu Tyr Asn Arg Pro Leu Leu Ala Asn Asp Leu Met Leu Ile  
 1 5 10 15

<210> 511  
 <211> 15  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 511

Tyr His Pro Ser Met Phe Cys Ala Gly Gly Gly Gln Asp Gln Lys  
 1 5 10 15

175

<210> 512  
 <211> 15  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 512  
 Asp Ser Gly Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu  
 1 5 10 15

<210> 513  
 <211> 15  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 513  
 Ala Pro Cys Gly Gln Val Gly Val Pro Asx Val Tyr Thr Asn Leu  
 1 5 10 15

<210> 514  
 <211> 15  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 514  
 Leu Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser  
 1 5 10 15

<210> 515  
 <211> 15  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 515  
 Met Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg  
 1 5 10 15

<210> 516  
 <211> 15  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 516  
 Val Ser Glu Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln



176

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1              5              10              15

<210> 517
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 517
Glu Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met
1              5              10              15

<210> 518
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 518
Arg Ala Glu Pro Gly Thr Glu Ala Arg Arg His Tyr Asp Glu Gly
1              5              10              15

<210> 519
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 519
Arg Ala Glu Pro Gly Thr Glu Ala Arg Arg Asn Tyr Asp Glu Gly Cys
1              5              10              15
Gly

<210> 520
<211> 25
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 520
Val Gly Glu Gly Leu Tyr Gln Gly Val Pro Arg Ala Glu Pro Gly Thr
1              5              10              15
Glu Ala Arg Arg His Tyr Asp Glu Gly
20              25

<210> 521
<211> 21
<212> PRT
<213> Artificial Sequence

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177

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 521

Ala	Pro	Phe	Pro	Asn	Gly	His	Val	Gly	Ala	Gly	Gly	Ser	Gly	Leu	Leu
1				5				10						15	
Pro	Pro	Pro	Pro	Ala											
				20											

&lt;210&gt; 522

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 522

Leu	Leu	Val	Val	Pro	Ala	Ile	Lys	Lys	Asp	Tyr	Gly	Ser	Gln	Glu	Asp
1				5					10					15	
Phe	Thr	Gln	Val												
				20											

&lt;210&gt; 523

&lt;211&gt; 254

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;220&gt;

&lt;221&gt; VARIANT

&lt;222&gt; (1)...(254)

&lt;223&gt; Xaa = any amino acid

&lt;400&gt; 523

Met	Ala	Thr	Ala	Gly	Asn	Pro	Trp	Gly	Trp	Phe	Leu	Gly	Tyr	Leu	Ile
1				5				10						15	
Leu	Gly	Val	Ala	Gly	Ser	Leu	Val	Ser	Gly	Ser	Cys	Ser	Gln	Ile	Ile
			20					25					30		
Asn	Gly	Glu	Asp	Cys	Ser	Pro	His	Ser	Gln	Pro	Trp	Gln	Ala	Ala	Leu
		35				40						45			
Val	Met	Glu	Asn	Glu	Leu	Phe	Cys	Ser	Gly	Val	Leu	Val	His	Pro	Gln
	50				55					60					
Trp	Val	Leu	Ser	Ala	Thr	His	Cys	Phe	Gln	Asn	Ser	Tyr	Thr	Ile	Gly
65				70					75					80	
Leu	Gly	Leu	His	Ser	Leu	Glu	Ala	Asp	Gln	Glu	Pro	Gly	Ser	Gln	Met
			85					90						95	
Val	Glu	Ala	Ser	Leu	Ser	Val	Arg	His	Pro	Glu	Tyr	Asn	Arg	Pro	Leu
			100					105					110		
Leu	Ala	Asn	Asp	Leu	Met	Leu	Ile	Lys	Leu	Asp	Glu	Ser	Val	Ser	Glu
		115				120						125			
Ser	Asp	Thr	Ile	Arg	Ser	Ile	Ser	Ile	Ala	Ser	Gln	Cys	Pro	Thr	Ala
	130					135					140				
Gly	Asn	Ser	Cys	Leu	Val	Ser	Gly	Trp	Gly	Leu	Leu	Ala	Asn	Gly	Arg
145					150					155					160

178

Met Pro Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu  
 165 170 175  
 Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys  
 180 185 190  
 Ala Gly Gly Gly Gln Xaa Gln Xaa Asp Ser Cys Asn Gly Asp Ser Gly  
 195 200 205  
 Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly  
 210 215 220  
 Lys Ala Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn Leu  
 225 230 235 240  
 Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser  
 245 250

<210> 524  
 <211> 765  
 <212> DNA  
 <213> Homo sapien

<400> 524  
 atggccacag caggaaatcc ctggggctgg ttcctggggt acctcatcct tgggtgtcgca 60  
 ggatcgctcg tctctggttag ctgcagccaa atcataaacg gcgaggactg cagcccgcac 120  
 tcgcagccct ggcaggcggc actggtcatg gaaaacgaat tggtctgctc gggcgctcctg 180  
 gtgcattcgc agtgggtgct gtcagccgca cactgtttcc agaactccta caccatcggg 240  
 ctgggcctgc acagtcttga ggccgaccaa gagccaggga gccagatggt ggaggccagc 300  
 ctctccgtac ggcaccacaga gtacaacaga cccttgctcg ctaacgacct catgctcatc 360  
 aagttggacg aatccgtgtc cgagtctgac accatccgga gcatcagcat tgcttcgcag 420  
 tgcctaccg cggggaactc ttgcctcgtt tctggctggg gtctgctggc gaacggcaga 480  
 atgcctaccg tgctgcagtg cgtgaacgtg tcggtggtgt ctgaggaggt ctgcagtaag 540  
 ctctatgacc cgctgtacca cccagcatg ttctgcgccg gcggagggca agaccagaag 600  
 gactcctgca acggtgactc tggggggccc ctgatctgca acgggtactt gcagggcctt 660  
 gtgtctttcg gaaaagcccc gtgtggccaa gttggcgtgc caggtgtcta caccaacctc 720  
 tgcaaattca ctgagtggat agagaaaacc gtccaggcca gttaa 765

<210> 525  
 <211> 254  
 <212> PRT  
 <213> Homo sapien

<400> 525  
 Met Ala Thr Ala Gly Asn Pro Trp Gly Trp Phe Leu Gly Tyr Leu Ile  
 1 5 10 15  
 Leu Gly Val Ala Gly Ser Leu Val Ser Gly Ser Cys Ser Gln Ile Ile  
 20 25 30  
 Asn Gly Glu Asp Cys Ser Pro His Ser Gln Pro Trp Gln Ala Ala Leu  
 35 40 45  
 Val Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln  
 50 55 60  
 Trp Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly  
 65 70 75 80  
 Leu Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met  
 85 90 95  
 Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu  
 100 105 110  
 Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu  
 115 120 125  
 Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala  
 130 135 140  
 Gly Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg

179

145					150					155				160
Met	Pro	Thr	Val	Leu	Gln	Cys	Val	Asn	Val	Ser	Val	Val	Ser	Glu
				165					170					175
Val	Cys	Ser	Lys	Leu	Tyr	Asp	Pro	Leu	Tyr	His	Pro	Ser	Met	Phe
			180					185					190	
Ala	Gly	Gly	Gly	Gln	Asp	Gln	Lys	Asp	Ser	Cys	Asn	Gly	Asp	Ser
	195						200					205		
Gly	Pro	Leu	Ile	Cys	Asn	Gly	Tyr	Leu	Gln	Gly	Leu	Val	Ser	Phe
	210					215					220			
Lys	Ala	Pro	Cys	Gly	Gln	Val	Gly	Val	Pro	Gly	Val	Tyr	Thr	Asn
225					230					235				240
Cys	Lys	Phe	Thr	Glu	Trp	Ile	Glu	Lys	Thr	Val	Gln	Ala	Ser	
				245					250					

&lt;210&gt; 526

&lt;211&gt; 963

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 526

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atgagttcct gcaacttcac acatgccacc tttgtgctta ttggtatccc aggattagag 60
aaagcccatt tctgggttgg cttccccctc ctttccatgt atgtagtggc aatgtttgga 120
aactgcacg tggtcttcat cgtaaggacg gaacgcagcc tgcacgctcc gatgtacctc 180
tttctctgca tgcttgacgc cattgacctg gccttatcca catccaccat gcctaagatc 240
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gccagattg gcatcgtggc tgtggtccgc ggatccctct ttttttccc actgcctctg 480
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caggatgtaa tgaagttggc ctatgcagac actttgccca atgtggtata tggctctact 600
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cgggtgctgg ctatgttcaa gatcagctgt gacaaggact tgcaggctgt gggaggcaag 960
tga
963

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&lt;210&gt; 527

&lt;211&gt; 320

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 527

Met	Ser	Ser	Cys	Asn	Phe	Thr	His	Ala	Thr	Phe	Val	Leu	Ile	Gly	Ile
				5					10					15	
Pro	Gly	Leu	Glu	Lys	Ala	His	Phe	Trp	Val	Gly	Phe	Pro	Leu	Leu	Ser
			20					25					30		
Met	Tyr	Val	Val	Ala	Met	Phe	Gly	Asn	Cys	Ile	Val	Val	Phe	Ile	Val
		35					40					45			
Arg	Thr	Glu	Arg	Ser	Leu	His	Ala	Pro	Met	Tyr	Leu	Phe	Leu	Cys	Met
	50					55					60				
Leu	Ala	Ala	Ile	Asp	Leu	Ala	Leu	Ser	Thr	Ser	Thr	Met	Pro	Lys	Ile
	65				70					75				80	
Leu	Ala	Leu	Phe	Trp	Phe	Asp	Ser	Arg	Glu	Ile	Ser	Phe	Glu	Ala	Cys
			85					90						95	
Leu	Thr	Gln	Met	Phe	Phe	Ile	His	Ala	Leu	Ser	Ala	Ile	Glu	Ser	Thr
			100					105					110		

180

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Ile Leu Leu Ala Met Ala Phe Asp Arg Tyr Val Ala Ile Cys His Pro
   115               120               125
Leu Arg His Ala Ala Val Leu Asn Asn Thr Val Thr Ala Gln Ile Gly
   130               135               140
Ile Val Ala Val Val Arg Gly Ser Leu Phe Phe Phe Pro Leu Pro Leu
  145               150               155               160
Leu Ile Lys Arg Leu Ala Phe Cys His Ser Asn Val Leu Ser His Ser
               165               170               175
Tyr Cys Val His Gln Asp Val Met Lys Leu Ala Tyr Ala Asp Thr Leu
               180               185               190
Pro Asn Val Val Tyr Gly Leu Thr Ala Ile Leu Leu Val Met Gly Val
   195               200               205
Asp Val Met Phe Ile Ser Leu Ser Tyr Phe Leu Ile Ile Arg Thr Val
  210               215               220
Leu Gln Leu Pro Ser Lys Ser Glu Arg Ala Lys Ala Phe Gly Thr Cys
  225               230               235               240
Val Ser His Ile Gly Val Val Leu Ala Phe Tyr Val Pro Leu Ile Gly
               245               250               255
Leu Ser Val Val His Arg Phe Gly Asn Ser Leu His Pro Ile Val Arg
               260               265               270
Val Val Met Gly Asp Ile Tyr Leu Leu Leu Pro Pro Val Ile Asn Pro
  275               280               285
Ile Ile Tyr Gly Ala Lys Thr Lys Gln Ile Arg Thr Arg Val Leu Ala
  290               295               300
Met Phe Lys Ile Ser Cys Asp Lys Asp Leu Gln Ala Val Gly Gly Lys
  305               310               315               320

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<210> 528
<211> 20
<212> DNA
<213> Homo Sapien

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20

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<210> 529
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<212> DNA
<213> Homo Sapien

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20

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<210> 530
<211> 1852
<212> DNA
<213> Homo sapiens

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181

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&lt;210&gt; 531

&lt;211&gt; 879

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 531

```

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&lt;210&gt; 532

&lt;211&gt; 292

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 532

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Met His Leu Ser Phe Pro Ala Phe Leu Pro Pro Trp Met Asp Arg Gly
          5              10              15
Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp His Asn Asp Ser Ser
          20              25              30
Val Lys Thr Leu Gly Ser Lys Arg Cys Lys Trp Cys Cys His Cys Phe
          35              40              45
Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val Val Ala Trp Gly Asp

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182

```

      50      55      60
Tyr Asp Asp Ser Ala Phe Met Asp Pro Arg Tyr His Val His Gly Glu
 65      70      75      80
Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp Gly Lys Val Pro Arg
      85      90      95
Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys Arg Asp
      100      105      110
Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly Asn Ser
      115      120      125
Glu Val Val Lys Leu Val Leu Asp Arg Arg Cys Gln Leu Asn Val Leu
      130      135      140
Asp Asn Lys Lys Arg Thr Ala Leu Thr Lys Ala Val Gln Cys Gln Glu
145      150      155      160
Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro Asn Ile
      165      170      175
Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Val Tyr Asn Glu
      180      185      190
Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu
      195      200      205
Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu Leu Gly Ile His Glu
      210      215      220
Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu
225      230      235      240
Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu Ile Leu Ala Val Cys
      245      250      255
Cys Gly Ser Ala Ser Ile Val Ser Pro Leu Leu Glu Gln Asn Val Asp
      260      265      270
Val Ser Ser Gln Asp Leu Glu Arg Arg Pro Glu Ser Met Leu Phe Leu
      275      280      285
Val Ile Ile Met
290

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<210> 533  
 <211> 801  
 <212> DNA  
 <213> Homo sapiens

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801

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<210> 534  
 <211> 266  
 <212> PRT  
 <213> Homo sapiens

183

&lt;400&gt; 534

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Arg Lys Gln Ala Ala Gly Ser Gly Ala Gly Tyr Ala Leu Pro Ser Ala
      20              25              30
Leu Gln Ser Met Pro Gln Gly Ser Tyr Ala Thr Ala Arg Phe Leu Val
      35              40              45
Ala Lys Arg Pro Thr Thr Gly His Leu Glu Lys Glu Phe Met Phe His
      50              55              60
Cys Arg Lys Gln Pro Gly Ser Pro Ser Arg Gly Leu Gly Leu Leu Trp
      65              70              75              80
Pro Trp Pro Asp Ile Glu Phe Val Pro Arg Gln Asp Lys Leu Thr Gln
      85              90              95
Ser Ser Val Leu Val Pro Gln Ile Cys Ala Cys Gln Thr Arg Pro Asn
      100             105             110
Trp Leu Asn Glu Gln Pro Ala Thr Ser Ala Gly Val Arg Leu Glu Glu
      115             120             125
Val Asp Gln Pro Pro Thr Leu Pro Ser Gln Gly Ser Gly Trp Pro Cys
      130             135             140
Ser His Ser Leu Ser Gly Cys His Leu Met Ala Asp Ile Ala Lys Ala
      145             150             155             160
Leu Gly Lys Ala Asp Gly Pro Trp Pro Tyr Leu Phe Val Arg Arg Thr
      165             170             175
Asp Val Pro Cys Pro Ala Ala Ser Glu Val Gly Gly Cys Ala Pro Ser
      180             185             190
Ser Trp His Thr Leu Ala Glu Val Thr Gly Cys Ser Leu Ser Pro Leu
      195             200             205
Ser Leu Ala Gln His Ala Gln Ala Ser Val Leu Leu Leu Cys Tyr Lys
      210             215             220
Trp Ser His Ile Gly Glu Thr Ser Ser His Leu Arg Ser Lys Val Tyr
      225             230             235             240
Ala Ala Phe Gly Gly Ser Ser Pro Cys Leu Lys Gly Leu Met Ser Leu
      245             250             255
Trp Ala Ser Trp Leu Pro Arg Gly Arg Pro
      260             265

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&lt;210&gt; 535

&lt;211&gt; 6082

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 535

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185

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&lt;211&gt; 6140

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

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&lt;223&gt; n=A,T,C or G

&lt;400&gt; 536

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&lt;210&gt; 537

&lt;211&gt; 1228

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 537

```

Met Leu Pro Val Tyr Gln Glu Val Lys Pro Asn Pro Leu Gln Asp Ala
      5              10              15
Asn Leu Cys Ser Arg Val Phe Phe Trp Trp Leu Asn Pro Leu Phe Lys
      20              25              30
Ile Gly His Lys Arg Arg Leu Glu Asp Asp Met Tyr Ser Val Leu
      35              40              45
Pro Glu Asp Arg Ser Gln His Leu Gly Glu Glu Leu Gln Gly Phe Trp
      50              55              60
Asp Lys Glu Val Leu Arg Ala Glu Asn Asp Ala Gln Lys Pro Ser Leu
      65              70              75              80
Thr Arg Ala Ile Ile Lys Cys Tyr Trp Lys Ser Tyr Leu Val Leu Gly
      85              90              95
Ile Phe Thr Leu Ile Glu Glu Ser Ala Lys Val Ile Gln Pro Ile Phe
      100             105             110
Leu Gly Lys Ile Ile Asn Tyr Phe Glu Asn Tyr Asp Pro Met Asp Ser
      115             120             125
Val Ala Leu Asn Thr Ala Tyr Ala Tyr Ala Thr Val Leu Thr Phe Cys
      130             135             140
Thr Leu Ile Leu Ala Ile Leu His His Leu Tyr Phe Tyr His Val Gln
      145             150             155             160
Cys Ala Gly Met Arg Leu Arg Val Ala Met Cys His Met Ile Tyr Arg
      165             170             175

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Lys Ala Leu Arg Leu Ser Asn Met Ala Met Gly Lys Thr Thr Thr Gly  
 180 185 190  
 Gln Ile Val Asn Leu Leu Ser Asn Asp Val Asn Lys Phe Asp Gln Val  
 195 200 205  
 Thr Val Phe Leu His Phe Leu Trp Ala Gly Pro Leu Gln Ala Ile Ala  
 210 215 220  
 Val Thr Ala Leu Leu Trp Met Glu Ile Gly Ile Ser Cys Leu Ala Gly  
 225 230 235 240  
 Met Ala Val Leu Ile Ile Leu Leu Pro Leu Gln Ser Cys Phe Gly Lys  
 245 250 255  
 Leu Phe Ser Ser Leu Arg Ser Lys Thr Ala Thr Phe Thr Asp Ala Arg  
 260 265 270  
 Ile Arg Thr Met Asn Glu Val Ile Thr Gly Ile Arg Ile Ile Lys Met  
 275 280 285  
 Tyr Ala Trp Glu Lys Ser Phe Ser Asn Leu Ile Thr Asn Leu Arg Lys  
 290 295 300  
 Lys Glu Ile Ser Lys Ile Leu Arg Ser Ser Cys Leu Arg Gly Met Asn  
 305 310 315 320  
 Leu Ala Ser Phe Phe Ser Ala Ser Lys Ile Ile Val Phe Val Thr Phe  
 325 330 335  
 Thr Thr Tyr Val Leu Leu Gly Ser Val Ile Thr Ala Ser Arg Val Phe  
 340 345 350  
 Val Ala Val Thr Leu Tyr Gly Ala Val Arg Leu Thr Val Thr Leu Phe  
 355 360 365  
 Phe Pro Ser Ala Ile Glu Arg Val Ser Glu Ala Ile Val Ser Ile Arg  
 370 375 380  
 Arg Ile Gln Thr Phe Leu Leu Asp Glu Ile Ser Gln Arg Asn Arg  
 385 390 395 400  
 Gln Leu Pro Ser Asp Gly Lys Lys Met Val His Val Gln Asp Phe Thr  
 405 410 415  
 Ala Phe Trp Asp Lys Ala Ser Glu Thr Pro Thr Leu Gln Gly Leu Ser  
 420 425 430  
 Phe Thr Val Arg Pro Gly Glu Leu Leu Ala Val Val Gly Pro Val Gly  
 435 440 445  
 Ala Gly Lys Ser Ser Leu Leu Ser Ala Val Leu Gly Glu Leu Ala Pro  
 450 455 460  
 Ser His Gly Leu Val Ser Val His Gly Arg Ile Ala Tyr Val Ser Gln  
 465 470 475 480  
 Gln Pro Trp Val Phe Ser Gly Thr Leu Arg Ser Asn Ile Leu Phe Gly  
 485 490 495  
 Lys Lys Tyr Glu Lys Glu Arg Tyr Glu Lys Val Ile Lys Ala Cys Ala  
 500 505 510  
 Leu Lys Lys Asp Leu Gln Leu Leu Glu Asp Gly Asp Leu Thr Val Ile  
 515 520 525  
 Gly Asp Arg Gly Thr Thr Leu Ser Gly Gly Gln Lys Ala Arg Val Asn  
 530 535 540  
 Leu Ala Arg Ala Val Tyr Gln Asp Ala Asp Ile Tyr Leu Leu Asp Asp  
 545 550 555 560  
 Pro Leu Ser Ala Val Asp Ala Glu Val Ser Arg His Leu Phe Glu Leu  
 565 570 575  
 Cys Ile Cys Gln Ile Leu His Glu Lys Ile Thr Ile Leu Val Thr His  
 580 585 590  
 Gln Leu Gln Tyr Leu Lys Ala Ala Ser Gln Ile Leu Ile Leu Lys Asp  
 595 600 605  
 Gly Lys Met Val Gln Lys Gly Thr Tyr Thr Glu Phe Leu Lys Ser Gly  
 610 615 620  
 Ile Asp Phe Gly Ser Leu Leu Lys Lys Asp Asn Glu Glu Ser Glu Gln  
 625 630 635 640

189

Pro	Pro	Val	Pro	Gly	Thr	Pro	Thr	Leu	Arg	Asn	Arg	Thr	Phe	Ser	Glu	645	650	655
Ser	Ser	Val	Trp	Ser	Gln	Gln	Ser	Ser	Arg	Pro	Ser	Leu	Lys	Asp	Gly	660	665	670
Ala	Leu	Glu	Ser	Gln	Asp	Thr	Glu	Asn	Val	Pro	Val	Thr	Leu	Ser	Glu	675	680	685
Glu	Asn	Arg	Ser	Glu	Gly	Lys	Val	Gly	Phe	Gln	Ala	Tyr	Lys	Asn	Tyr	690	695	700
Phe	Arg	Ala	Gly	Ala	His	Trp	Ile	Val	Phe	Ile	Phe	Leu	Ile	Leu	Leu	705	710	715
Asn	Thr	Ala	Ala	Gln	Val	Ala	Tyr	Val	Leu	Gln	Asp	Trp	Trp	Leu	Ser	720	725	730
Tyr	Trp	Ala	Asn	Lys	Gln	Ser	Met	Leu	Asn	Val	Thr	Val	Asn	Gly	Gly	735	740	745
Gly	Asn	Val	Thr	Glu	Lys	Leu	Asp	Leu	Asn	Trp	Tyr	Leu	Gly	Ile	Tyr	750	755	760
Ser	Gly	Leu	Thr	Val	Ala	Thr	Val	Leu	Phe	Gly	Ile	Ala	Arg	Ser	Leu	765	770	775
Leu	Val	Phe	Tyr	Val	Leu	Val	Asn	Ser	Ser	Gln	Thr	Leu	His	Asn	Lys	780	785	790
Met	Phe	Glu	Ser	Ile	Leu	Lys	Ala	Pro	Val	Leu	Phe	Phe	Asp	Arg	Asn	795	800	805
Pro	Ile	Gly	Arg	Ile	Leu	Asn	Arg	Phe	Ser	Lys	Asp	Ile	Gly	His	Leu	810	815	820
Asp	Asp	Leu	Leu	Pro	Leu	Thr	Phe	Leu	Asp	Phe	Ile	Gln	Thr	Leu	Leu	825	830	835
Gln	Val	Val	Gly	Val	Val	Ser	Val	Ala	Val	Ala	Val	Ile	Pro	Trp	Ile	840	845	850
Ala	Ile	Pro	Leu	Val	Pro	Leu	Gly	Ile	Ile	Phe	Ile	Phe	Leu	Arg	Arg	855	860	865
Tyr	Phe	Leu	Glu	Thr	Ser	Arg	Asp	Val	Lys	Arg	Leu	Glu	Ser	Thr	Thr	870	875	880
Arg	Ser	Pro	Val	Phe	Ser	His	Leu	Ser	Ser	Ser	Leu	Gln	Gly	Leu	Trp	885	890	895
Thr	Ile	Arg	Ala	Tyr	Lys	Ala	Glu	Glu	Arg	Cys	Gln	Glu	Leu	Phe	Asp	900	905	910
Ala	His	Gln	Asp	Leu	His	Ser	Glu	Ala	Trp	Phe	Leu	Phe	Leu	Thr	Thr	915	920	925
Ser	Arg	Trp	Phe	Ala	Val	Arg	Leu	Asp	Ala	Ile	Cys	Ala	Met	Phe	Val	930	935	940
Ile	Ile	Val	Ala	Phe	Gly	Ser	Leu	Ile	Leu	Ala	Lys	Thr	Leu	Asp	Ala	945	950	955
Gly	Gln	Val	Gly	Leu	Ala	Leu	Ser	Tyr	Ala	Leu	Thr	Leu	Met	Gly	Met	960	965	970
Phe	Gln	Trp	Cys	Val	Arg	Gln	Ser	Ala	Glu	Val	Glu	Asn	Met	Met	Ile	975	980	985
Ser	Val	Glu	Arg	Val	Ile	Glu	Tyr	Thr	Asp	Leu	Glu	Lys	Glu	Ala	Pro	990	995	1000
Trp	Glu	Tyr	Gln	Lys	Arg	Pro	Pro	Pro	Ala	Trp	Pro	His	Glu	Gly	Val	1005	1010	1015
Ile	Ile	Phe	Asp	Asn	Val	Asn	Phe	Met	Tyr	Ser	Pro	Gly	Gly	Pro	Leu	1020	1025	1030
Val	Leu	Lys	His	Leu	Thr	Ala	Leu	Ile	Lys	Ser	Gln	Glu	Lys	Val	Gly	1035	1040	1045
Ile	Val	Gly	Arg	Thr	Gly	Ala	Gly	Lys	Ser	Ser	Leu	Ile	Ser	Ala	Leu	1050	1055	1060
Phe	Arg	Leu	Ser	Glu	Pro	Glu	Gly	Lys	Ile	Trp	Ile	Asp	Lys	Ile	Leu	1065	1070	1075
																1080	1085	1090
																1095	1100	

190

Thr Thr Glu Ile Gly Leu His Asp Leu Arg Lys Lys Met Ser Ile Ile  
 1105 1110 1115 1120  
 Pro Gln Glu Pro Val Leu Phe Thr Gly Thr Met Arg Lys Asn Leu Asp  
 1125 1130 1135  
 Pro Phe Asn Glu His Thr Asp Glu Glu Leu Trp Asn Ala Leu Gln Glu  
 1140 1145 1150  
 Val Gln Leu Lys Glu Thr Ile Glu Asp Leu Pro Gly Lys Met Asp Thr  
 1155 1160 1165  
 Glu Leu Ala Glu Ser Gly Ser Asn Phe Ser Val Gly Gln Arg Gln Leu  
 1170 1175 1180  
 Val Cys Leu Ala Arg Ala Ile Leu Arg Lys Asn Gln Ile Leu Ile Ile  
 1185 1190 1195 1200  
 Asp Glu Ala Thr Ala Asn Val Asp Pro Arg Thr Asp Glu Leu Ile Gln  
 1205 1210 1215  
 Lys Lys Ser Gly Arg Asn Leu Pro Thr Ala Pro Cys  
 1220 1225

&lt;210&gt; 538

&lt;211&gt; 1261

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 538

Met Tyr Ser Val Leu Pro Glu Asp Arg Ser Gln His Leu Gly Glu Glu  
 5 10 15  
 Leu Gln Gly Phe Trp Asp Lys Glu Val Leu Arg Ala Glu Asn Asp Ala  
 20 25 30  
 Gln Lys Pro Ser Leu Thr Arg Ala Ile Ile Lys Cys Tyr Trp Lys Ser  
 35 40 45  
 Tyr Leu Val Leu Gly Ile Phe Thr Leu Ile Glu Glu Ser Ala Lys Val  
 50 55 60  
 Ile Gln Pro Ile Phe Leu Gly Lys Ile Ile Asn Tyr Phe Glu Asn Tyr  
 65 70 75 80  
 Asp Pro Met Asp Ser Val Ala Leu Asn Thr Ala Tyr Ala Tyr Ala Thr  
 85 90 95  
 Val Leu Thr Phe Cys Thr Leu Ile Leu Ala Ile Leu His His Leu Tyr  
 100 105 110  
 Phe Tyr His Val Gln Cys Ala Gly Met Arg Leu Arg Val Ala Met Cys  
 115 120 125  
 His Met Ile Tyr Arg Lys Ala Leu Arg Leu Ser Asn Met Ala Met Gly  
 130 135 140  
 Lys Thr Thr Thr Gly Gln Ile Val Asn Leu Leu Ser Asn Asp Val Asn  
 145 150 155 160  
 Lys Phe Asp Gln Val Thr Val Phe Leu His Phe Leu Trp Ala Gly Pro  
 165 170 175  
 Leu Gln Ala Ile Ala Val Thr Ala Leu Leu Trp Met Glu Ile Gly Ile  
 180 185 190  
 Ser Cys Leu Ala Gly Met Ala Val Leu Ile Ile Leu Leu Pro Leu Gln  
 195 200 205  
 Ser Cys Phe Gly Lys Leu Phe Ser Ser Leu Arg Ser Lys Thr Ala Thr  
 210 215 220  
 Phe Thr Asp Ala Arg Ile Arg Thr Met Asn Glu Val Ile Thr Gly Ile  
 225 230 235 240  
 Arg Ile Ile Lys Met Tyr Ala Trp Glu Lys Ser Phe Ser Asn Leu Ile  
 245 250 255  
 Thr Asn Leu Arg Lys Lys Glu Ile Ser Lys Ile Leu Arg Ser Ser Cys  
 260 265 270  
 Leu Arg Gly Met Asn Leu Ala Ser Phe Phe Ser Ala Ser Lys Ile Ile

[illegible]





193

				1205					1210				1215		
Val	Leu	Leu	Gln	Asn	Lys	Glu	Ser	Leu	Phe	Tyr	Lys	Met	Val	Gln	Gln
			1220						1225				1230		
Leu	Gly	Lys	Ala	Glu	Ala	Ala	Ala	Leu	Thr	Glu	Thr	Ala	Lys	Gln	Arg
		1235						1240					1245		
Trp	Gly	Phe	Thr	Met	Leu	Ala	Arg	Leu	Val	Ser	Asn	Ser			
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<210> 539  
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 <212> PRT  
 <213> Artificial Sequence

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 <223> Made in a lab

<400> 539  
 Cys Leu Ser His Ser Val Ala Val Val Thr  
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<210> 540  
 <211> 9  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 540  
 Ala Val Val Thr Ala Ser Ala Ala Leu  
 1 5

<210> 541  
 <211> 14  
 <212> PRT  
 <213> Homo sapiens

<400> 541  
 Leu Ala Gly Leu Leu Cys Pro Asp Pro Arg Pro Leu Glu Leu  
 5 10

<210> 542  
 <211> 15  
 <212> PRT  
 <213> Homo sapiens

<400> 542  
 Thr Gln Val Val Phe Asp Lys Ser Asp Leu Ala Lys Tyr Ser Ala  
 5 10 15

<210> 543  
 <211> 12  
 <212> PRT  
 <213> Homo sapiens

<400> 543  
 Phe Met Gly Ser Ile Val Gln Leu Ser Gln Ser Val  
 5 10

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<210> 544
<211> 18
<212> PRT
<213> Homo sapiens
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```

<400> 544
Thr Tyr Val Pro Pro Leu Leu Leu Glu Val Gly Val Glu Glu Lys Phe
          5                      10                      15
Met Thr

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```
<210> 545
<211> 18
<212> PRT
<213> Homo sapiens
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```
<400> 545
Met Asp Arg Leu Val Gln Arg Phe Gly Thr Arg Ala Val Tyr Leu Ala
      5              10              15
Ser Val
```

```
<210> 546
<211> 29
<212> PRT
<213> Homo sapiens
```

```

<400> 546
Phe Val Gly Glu Gly Leu Tyr Gln Gly Val Pro Arg Ala Glu Pro Gly
                    5                      10                      15
Thr Glu Ala Arg Arg His Tyr Asp Glu Gly Val Arg Met
          20                      25

```

```
<210> 547
<211> 58
<212> PRT
<213> Homo sapiens
```

```

<400> 547
Val Ala Glu Glu Ala Ala Leu Gly Pro Thr Glu Pro Ala Glu Gly Leu
              5                      10                      15
Ser Ala Pro Ser Leu Ser Pro His Cys Cys Pro Cys Arg Ala Arg Leu
              20                      25                      30
Ala Phe Arg Asn Leu Gly Ala Leu Leu Pro Arg Leu His Gln Leu Cys
              35                      40                      45
Cys Arg Met Pro Arg Thr Leu Arg Arg Leu
              50                      55

```

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<210> 548
<211> 18
<212> PRT
<213> Homo sapiens
```

<400> 548  
Ile Asp Trp Asp Thr Ser Ala Leu Ala Pro Tyr Leu Gly Thr Gln Glu

	5	10	15
Glu Cys			
<210> 549			
<211> 18			
<212> PRT			
<213> Homo sapiens			
<400> 549			
Leu Glu Ala Leu Leu Ser Asp Leu Phe Arg Asp Pro Asp His Cys Arg			
	5	10	15
Gln Ala			

<400> 550  
Ser Asp His Trp Arg Gly Arg Tyr Gly Arg Arg Arg Pro Phe  
                          5                          10

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<210> 551
<211> 11
<212> PRT
<213> Artificial Sequence
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<220>  
<223> Made in a lab

<400> 551  
Phe Asp Lys Ser Asp Leu Ala Lys Tyr Ser Ala  
5 10

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<210> 552
<211> 2577
<212> DNA
<213> Homo sapiens
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400> 552						
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&lt;210&gt; 553

&lt;211&gt; 58

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 553

```

Ser Ile Cys Asn Met Thr Cys Ala Ser Val Phe Phe Cys Asp Gln Lys
              5              10              15
Phe Leu Thr Phe Ser Phe Leu Ser Met Val Glu Pro Pro Arg Ala Gly
              20              25              30
Val Leu Asn Ser Gln Ala Thr Asp Ser Tyr Gln Ser Thr Asp Tyr Tyr
              35              40              45
Glu Pro His His Thr Gly Gly Gly Glu His
              50              55

```

&lt;210&gt; 554

&lt;211&gt; 59

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 554

```

Leu Gln Lys Asn Lys Leu Arg Ala Ser Thr Asp Ser Thr Leu Trp Ile
              5              10              15
Cys Ala Ala Glu Ala Ser Thr Lys Pro Tyr Phe Tyr Thr Cys Leu Val
              20              25              30
Met Leu His Gly Gln Gly Leu Ala Leu Leu Ser Pro Thr Asn Leu Pro
              35              40              45
Glu Ile Leu Arg Phe Leu Phe Asn Gly Phe Leu
              50              55

```

197

<210> 555  
 <211> 71  
 <212> PRT  
 <213> Homo sapiens

<400> 555  
 Leu Gly Arg Phe Ser Leu Ser Cys Lys Ser Gly His Ser Arg Gly Gln  
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 Pro Gln Leu Gly Ala Thr Ala Gln Gly Lys Val His Met Gly Leu Ser  
                   20                  25                  30  
 Thr Ala Gln Gly Ser Ile Gln Asp Ile Lys Val Pro His Ser Ile Asp  
                   35                  40                  45  
 Leu Val Ala Lys Lys Lys Lys Gln Thr Leu Ile Ser Phe Cys His Pro  
                   50                  55                  60  
 Ser Asp Pro Leu Glu Leu Leu  
                   65                  70

<210> 556  
 <211> 81  
 <212> PRT  
 <213> Homo sapiens

<400> 556  
 Asn His Pro Glu Gln Gly Ser Ser Thr Pro Arg Pro Gln Thr His Thr  
                   5                  10                  15  
 Ser Pro Arg Thr Ile Met Asn His Thr Thr Gln Glu Glu Val Ser Thr  
                   20                  25                  30  
 Arg Gln Ala Lys Glu Ala Ser Pro Val Leu Thr Ala Thr Arg His Gly  
                   35                  40                  45  
 Ser Tyr Tyr Ser Leu Asn Ser Ala Ser Thr Gln Ile Ser Asp Asn Ile  
                   50                  55                  60  
 Arg Asn Ser Leu Glu His Glu Pro Cys Cys Glu Leu Pro Ile Arg Arg  
                   65                  70                  75                  80  
 Ile

<210> 557  
 <211> 54  
 <212> PRT  
 <213> Homo sapiens

<400> 557  
 Ser Leu Ser Ala Thr Pro Leu Thr Leu Trp Asn Ser Ser Asp Pro Leu  
                   5                  10                  15  
 Glu Gln Ala Tyr Leu Ile Ser Ala Arg Glu Lys Thr Asn Asn Gly Leu  
                   20                  25                  30  
 Lys Gly Ser Leu Thr Met Lys Val Ser Ala Asn Ser Trp Leu Arg Cys  
                   35                  40                  45  
 Gly Phe His Ile Arg Phe  
                   50

<210> 558  
 <211> 77  
 <212> PRT  
 <213> Homo sapiens

198

&lt;220&gt;

&lt;221&gt; VARIANT

&lt;222&gt; (1)...(77)

&lt;223&gt; Xaa = Any amino acid

&lt;400&gt; 558

```

Asn Asp Arg Asp Arg Asn Ser Asn Lys Val Ile Xaa Lys Ala Asn Leu
              5              10              15
Ile Tyr Phe Thr Asn Leu Thr Ser Cys Leu Ser Val Gln Asn Gln Thr
              20              25              30
Phe Thr Cys Thr Lys Arg His Lys His Leu Gln Cys Ser Ser Val His
              35              40              45
Leu Cys Lys Ile Pro Pro Arg Leu Lys Gly Arg Asp Lys Lys Lys Lys
              50              55              60
Pro Ser Tyr Leu Ser Gly Val Leu His Ser Arg Ser Tyr
              65              70              75

```

&lt;210&gt; 559

&lt;211&gt; 50

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 559

```

Thr Leu Pro Pro Leu Arg Ser Val Ile Thr Leu Glu Thr His Trp Ser
              5              10              15
Thr Asn Pro Val Val Asn Cys Leu Ser Glu Gly Ser Arg Leu Cys Ala
              20              25              30
Ser Tyr Glu Asn Leu Met Pro Asp Asp Leu Ser Leu Ser His Phe Ala
              35              40              45
Pro Arg
              50

```

&lt;210&gt; 560

&lt;211&gt; 56

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 560

```

Ile Gly Ser Leu Lys Gly Pro Thr Thr Ala Gly Ser His Cys Ser Gly
              5              10              15
Glu Gly Ser Tyr Gly Thr Phe Tyr Cys Pro Arg Phe Tyr Thr Gly Tyr
              20              25              30
Lys Gly Ala Ser Gln Tyr Arg Ser Gly Ser Lys Glu Glu Glu Thr Asn
              35              40              45
Thr Asp Leu Phe Leu Pro Pro Leu
              50              55

```

&lt;210&gt; 561

&lt;211&gt; 57

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; VARIANT

199

&lt;222&gt; (1)...(57)

&lt;223&gt; Xaa = Any amino acid

&lt;400&gt; 561

Val	Leu	His	Leu	Asp	Gln	Met	Asn	Asn	Val	Gly	Ile	Xaa	Met	Asp	Lys
				5					10					15	
Gly	Leu	Lys	Ser	Pro	Glu	Ile	Lys	Asn	Pro	Ala	Pro	Thr	Gly	Thr	Ser
			20					25					30		
Asn	Leu	Ser	Cys	Phe	Leu	Ser	Xaa	Phe	Trp	Leu	Met	Gln	Gly	Thr	Asn
		35					40					45			
Ser	Leu	Pro	Arg	Glu	Asn	Tyr	Leu	Asn							
	50					55									

&lt;210&gt; 562

&lt;211&gt; 59

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; VARIANT

&lt;222&gt; (1)...(59)

&lt;223&gt; Xaa = Any amino acid

&lt;400&gt; 562

Asp	Leu	Tyr	Pro	Xaa	Arg	Ser	Gln	His	Cys	Ser	Phe	Asp	Pro	Ser	Val
				5					10					15	
Ala	Pro	Met	His	Gly	Ile	Lys	Asn	Ser	Ile	Thr	Ser	Leu	Ile	Phe	Leu
			20				25						30		
Ile	Ser	Tyr	Leu	Xaa	Leu	Glu	Met	Ser	Ser	Leu	Ser	Glu	Ser	Leu	Val
		35				40						45			
Leu	Ser	Ser	Gly	Asp	Tyr	Val	Leu	Asp	Thr	Pro					
	50					55									

&lt;210&gt; 563

&lt;211&gt; 79

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 563

Cys	Phe	Leu	Phe	Pro	Tyr	Leu	Trp	Leu	Tyr	Ala	Gln	Pro	Leu	Phe	Pro
				5					10					15	
Lys	Gln	Gln	Pro	Pro	Ala	Leu	Ala	Pro	Gly	His	Pro	Asp	Phe	Ile	His
			20					25					30		
Thr	Gln	Asn	Glu	Gln	Ile	Asp	Pro	Ser	Pro	His	Ile	Gln	Asn	Leu	Met
		35				40					45				
Trp	Asn	Pro	His	Leu	Ser	Gln	Glu	Leu	Ala	Glu	Thr	Phe	Met	Val	Arg
	50					55				60					
Asp	Pro	Leu	Arg	Pro	Leu	Leu	Val	Phe	Ser	Leu	Ala	Asp	Ile	Arg	
	65				70					75					

&lt;210&gt; 564

&lt;211&gt; 64

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 564



200

Ala Cys Ser Lys Gly Ser Glu Glu Phe Gln Arg Val Arg Gly Val Ala  
                                   5                                  10                                  15  
 Glu Arg Asp Gln Cys Leu Phe Leu Leu Leu Cys Tyr Gln Ile Tyr Thr  
                                   20                                  25                                  30  
 Val Arg His Leu Tyr Ile Leu Tyr Arg Thr Leu Gly Ser Arg Lys Ser  
                                   35                                  40                                  45  
 His Met Asn Leu Pro Leu Ser Ser Gly Ser Gln Leu Trp Leu Ala Pro  
                                   50                                  55                                  60

&lt;210&gt; 565

&lt;211&gt; 57

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; VARIANT

&lt;222&gt; (1)...(57)

&lt;223&gt; Xaa = Any amino acid

&lt;400&gt; 565

Leu Tyr Tyr Cys Ser Tyr Leu Cys His Phe Arg Thr Ala Leu Ile Leu  
                                   5                                  10                                  15  
 Ala Val Cys Cys Gly Ser Ala Ser Ile Val Ser Leu Leu Leu Glu Gln  
                                   20                                  25                                  30  
 Asn Ile Asp Val Ser Ser Gln Asp Leu Ser Gly Gln Thr Ala Arg Glu  
                                   35                                  40                                  45  
 Tyr Ala Val Ser Ser Xaa His Asn Val  
                                   50                                  55

&lt;210&gt; 566

&lt;211&gt; 55

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 566

Ile Leu Leu Glu Phe Phe Arg Asn Gln Arg Gly Ser Leu Asn Pro Arg  
                                   5                                  10                                  15  
 Lys Thr Val Pro Phe Ile Lys Ser Glu Gly Gly Glu Lys Lys Gly His  
                                   20                                  25                                  30  
 Cys Asn His Ser Val Val Ser Ile Asp Ser Ala Ala Ala Leu Leu Pro  
                                   35                                  40                                  45  
 Leu Lys Leu Val Leu Leu Pro  
                                   50                                  55

&lt;210&gt; 567

&lt;211&gt; 51

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 567

Tyr Ser Asp Phe Asp Val Phe Cys Ser His Thr Tyr Gly Tyr Met Leu  
                                   5                                  10                                  15  
 Ser His Cys Ser Gln Ser Ser Ser Pro Leu Leu Trp Pro Leu Gly Ile  
                                   20                                  25                                  30  
 Leu Thr Leu Ser Thr His Lys Met Ser Lys Leu Thr Leu Pro Pro Ile

201

35  
Phe Arg Thr  
50

40

45

<210> 568  
<211> 75  
<212> PRT  
<213> Homo sapiens

<400> 568  
Lys Val Gly Glu Tyr Ile Leu Gln Ser Leu Leu Arg Ile Arg Lys Ile  
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Tyr Val Ala Phe Asn Ser Val Pro Ser Thr Cys Leu Leu Ala Ser Leu  
20 25 30  
Thr Glu Thr Pro Val Thr Thr Ile Leu Thr Ile Ile Ile Asn Leu Thr  
35 40 45  
Cys Phe Gln His Ala Glu Ser Tyr Leu Phe Tyr Pro Leu Ala Asp  
50 55 60  
Phe Leu Leu Gln His Ile Ser Leu Gly Lys Leu  
65 70 75

<210> 569  
<211> 4809  
<212> DNA  
<213> Homo sapiens

<400> 569  
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&lt;210&gt; 570

&lt;211&gt; 951

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 570

203

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aaaattgaat attgagatac cattcttttag tgttaccttt tttaccacaca tgtgttttctg 60
aaaatattgg aatttttattc atcttaaaaa ttggaccogg ccttattttac catctttaat 120
ccatttttagt actatgggtg agtacatgga attgaagtct ggcttaaadc ttcagaaagt 180
tatatatcta ttttatttta tttttttgag acagagtctc gctgtgtcac ccaggctgga 240
gtgcggtgcc acaatcttgg ctcaactgcaa cctctgagtc ccaggttcaa gcgatactca 300
tgcctcggcc tcctgagtag ctgggactac aggcgtgcac caccacatct ggctaattctt 360
tttttgtatt tttagtagag acgggggttc actgtggtct ccatctcctg acctcgtgat 420
ccgcctgcct cccaaagtgc tgggattaca ggcatgagcc accgcacaca gctgggactg 480
ggtaatttat aaagaaaaga ggtttaatga ctacagttc cgcattggctg gagaggcctc 540
aggaaactta caatcatggt ggaaggcgaa ggggaagcaa ggcacgtctt acatggtggc 600
aggagagaac gagtgagggg ggagactgcc aaaaactttt tttttttgag acaagagtct 660
ggcctgttg cccaggctgg agtgcagtg catgatctca gctcactgca acctctgcct 720
cagggttca agcaattctc atgcctcagc ctccgcata gctgggacca caggtaatgca 780
ccaccacacc tagctaattt ttgtagtttt agtagagatg ggggtctcact atgttgctca 840
ggctggtcta aaactcctgg gctccagcaa tccgcctgcc ttggcctccc aaagtgtctg 900
ggttacaggc ataagccacc acatccagcc tgccacatac ttttaaacta t 951

```

&lt;210&gt; 571

&lt;211&gt; 819

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 571

```

cagcttaaaa atggttttctt gaaatcagtg attagcattc actcaccagt acccctacta 60
aggggtaggc actggtttgt actcctggga atacaggagt acaccagaat ttattttctgc 120
ttattgcttt tggtgcaaact gccgtggctt catctgagga attctagaat tcagaggggtg 180
tagccctcca ctctgctgtc ttgctatctg ctctcattgc atccgtttaa cctgcattct 240
gaaagatggt tctcaggttt ttocctgacg attttcttct tttctgattc tgacaatgtt 300
ttaaatcatt gtactgtggt tatcatttct ctgcatttat tttaccatc ttcttttgta 360
acttgctcta ttgtctttta atttctgcct gttctttatg gctttcaact tcataaataa 420
catgttttct caaatctctt tgtgaattcc agagagggcc aggcacgggtg gctcacatct 480
gtaatcccag cactttgggg aggctgagac ggggtgatca cttgagggtca ggagtttgag 540
accagcctgg ccaacatggt gaaatcccgt ttcactaaaa atacaaaaat taccaggca 600
tggtggcggg cgctgtaat cccaggtaact cgggaggctg agggaggaga atcgcttgaa 660
cctgggaggg tgaggaggga gaatcgcttg aaccgggag gcagagggtg cagtgaaccg 720
agatcatggt gctgcactcc agcctggtca acagagcaag actctgcctc aaaaacaaac 780
aaataaacia acaaaciaac aaaacagaga gattttgct 819

```

&lt;210&gt; 572

&lt;211&gt; 203

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 572

```

tatagaatac tcaagctatg catcaagctt ggtaccgagc tcggatccac tatttacggc 60
cgccagtgtg ctggaattcg cccttagctc ggatccacta gtccagtgtg gtggaattcc 120
attgtgttgg gcccaacaca atggagccac cacatccagc ctgccacata cttttaaact 180
atcaggtctc atgagaactc atg 203

```

&lt;210&gt; 573

&lt;211&gt; 132

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 573

```

Met Val Glu Gly Glu Glu Ala Arg His Val Leu His Gly Gly Arg
          5              10              15
Arg Glu Arg Val Arg Gly Glu Thr Ala Thr Asn Phe Phe Phe Leu Arg

```

20							25					30				
Gln	Glu	Ser	Gly	Pro	Val	Ala	Gln	Ala	Gly	Val	Gln	Trp	His	Asp	Leu	
35							40			45						
Ser	Ser	Leu	Gln	Pro	Leu	Pro	His	Arg	Phe	Lys	Gln	Phe	Ser	Cys	Leu	
50							55			60						
Ser	Leu	Pro	His	Ser	Trp	Asp	His	Arg	Tyr	Ala	Pro	Pro	His	Leu	Ala	
65			70				75					80				
Asn	Phe	Cys	Ser	Phe	Ser	Arg	Asp	Gly	Val	Ser	Leu	Cys	Cys	Ser	Gly	
				85			90					95				
Trp	Ser	Lys	Thr	Pro	Gly	Leu	Gln	Gln	Ser	Ala	Cys	Leu	Gly	Leu	Pro	
			100			105					110					
Lys	Cys	Trp	Gly	Tyr	Arg	His	Lys	Pro	Pro	His	Pro	Ala	Cys	His	Ile	
115							120			125						
Leu	Leu	Asn	Tyr													
130																

```
<210> 574
<211> 62
<212> PRT
<213> Homo sapiens
```

<400> 574																
Met	Thr	His	Ser	Ser	Ala	Trp	Leu	Glu	Arg	Pro	Gln	Glu	Thr	Tyr	Asn	
				5					10						15	
His	Gly	Gly	Arg	Arg	Arg	Gly	Ser	Lys	Ala	Arg	Leu	Thr	Trp	Trp	Gln	
			20					25					30			
Glu	Arg	Thr	Ser	Glu	Gly	Gly	Asp	Cys	His	Lys	Leu	Phe	Phe	Phe	Glu	
		35					40					45				
Thr	Arg	Val	Trp	Pro	Cys	Cys	Pro	Gly	Trp	Ser	Ala	Val	Ala			
	50					55					60					

```
<210> 575
<211> 76
<212> PRT
<213> Homo sapiens
```

```

<400> 575
Met Val Lys Ser Arg Phe Thr Lys Asn Thr Lys Ile Thr Gln Ala Trp
                    5                      10                      15
Trp Arg Ala Pro Val Ile Pro Gly Thr Arg Glu Ala Glu Gly Gly Glu
                    20                      25                      30
Ser Leu Glu Pro Gly Arg Leu Arg Glu Glu Asn Arg Leu Asn Pro Gly
                    35                      40                      45
Gly Arg Gly Cys Ser Glu Pro Arg Ser Cys Cys Cys Thr Pro Ala Trp
                    50                      55                      60
Ser Thr Glu Gln Asp Ser Ala Ser Lys Thr Asn Lys
                    65                      70                      75

```

```
<210> 576
<211> 68
<212> PRT
<213> Homo sapiens
```

<220>  
<221> VARIANT

205

&lt;222&gt; (1)...(68)

&lt;223&gt; Xaa = Any Amino Acid

&lt;400&gt; 576

```

Met Leu Gly Lys Ser Arg Ala Val Cys Leu Pro Ser Thr Thr Val Thr
              5              10              15
Thr Val Cys Tyr Leu Ala Ser Ser Ser Ala Ser Arg Glu Thr Ala Thr
              20              25              30
Arg Gln Ala Pro Gly Asn Trp Lys Met Xaa Ser Lys Cys His Ala Gln
              35              40              45
Leu Leu Phe Thr Phe Tyr Leu Asn His Phe Tyr Gln Ile Arg Leu Asn
              50              55              60
Pro Gly Tyr Ser
65

```

&lt;210&gt; 577

&lt;211&gt; 57

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 577

```

Met Tyr Leu Glu Asn Ser Phe Tyr Cys Gln Met Ile Leu Leu Lys Arg
              5              10              15
Cys Arg Leu Ser Lys Ile Ser Thr Gln Arg Val Val Pro Asp Gly Pro
              20              25              30
Pro Ala Pro Val Pro Gly Ser Phe Pro Met Phe Pro Arg Phe Gly Phe
              35              40              45
Arg Leu Ala Pro Pro Ala Asp Thr Pro
              50              55

```

&lt;210&gt; 578

&lt;211&gt; 51

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 578

```

Met Gln Leu Ile Tyr Leu Cys Phe Leu Gly Leu Leu Tyr Ile Arg His
              5              10              15
His Asp Ser Gln Ser Phe Val Ile Leu Tyr Tyr Lys Lys Leu Asn Tyr
              20              25              30
Tyr Phe Lys Tyr Gly Gln Ile Arg Ala Phe His Ile Ala Lys Val Tyr
              35              40              45
Gln Pro His
50

```

&lt;210&gt; 579

&lt;211&gt; 56

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 579

```

Met His Phe Thr Phe Met Gln Leu Ile Tyr Leu Cys Phe Leu Gly Leu
              5              10              15
Leu Tyr Ile Arg His His Asp Ser Gln Ser Phe Val Ile Leu Tyr Tyr
              20              25              30
Lys Lys Leu Asn Tyr Tyr Phe Lys Tyr Gly Gln Ile Arg Ala Phe His
              35              40              45
Ile Ala Lys Val Tyr Gln Pro His

```

206

50

55

&lt;210&gt; 580

&lt;211&gt; 67

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 580

```

Met Glu Leu Arg Thr Lys Ala Leu Arg Thr Ala Gln Gln Leu Thr Ser
              5              10              15
Cys Val Thr Ala Leu Lys Ala Ala Gly Pro Pro Leu Thr Phe Trp Lys
              20              25              30
Gly Lys Trp Val Gln Cys Cys Leu Pro Leu Trp Gly Leu Leu Gly Ser
              35              40              45
His Ala Phe Tyr Ile Tyr Ala Val Asp Ile Phe Met Phe Pro Gly Ser
              50              55              60
Phe Ile His
              65

```

&lt;210&gt; 581

&lt;211&gt; 77

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 581

```

Met Leu Glu Val Lys Phe Glu Val Ser Leu Arg Pro Thr Gly Asn Glu
              5              10              15
Thr Ala Gly Gln Thr His Gly Thr Gln Asp Lys Gly Ser Lys Asp Ser
              20              25              30
Thr Ala Ala Asp Ile Leu Cys Asp Ser Leu Glu Ser Ser Arg Pro Ala
              35              40              45
Ala His Ile Leu Glu Gly Lys Met Gly Thr Met Leu Ser Ala Thr Leu
              50              55              60
Gly Pro Ser Trp Val Thr Cys Ile Leu His Leu Cys Ser
              65              70              75

```

&lt;210&gt; 582

&lt;211&gt; 51

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 582

```

Met Leu Phe Leu Gln Thr Ile Asp Thr Lys Cys Thr Gly Ile Glu Ile
              5              10              15
Asn Arg Asn Trp Ser Lys Val Trp His Thr His Ser His Val Asp Val
              20              25              30
Lys Leu Cys Leu Glu Phe Leu Cys Gly Val Trp Phe Gly Leu Gly Phe
              35              40              45
Leu Gly Val
              50

```

&lt;210&gt; 583

&lt;211&gt; 60

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 583

```

Met Ser Thr Ser Asp Gly Phe Ala Pro Pro Pro Gln Leu Gly Ser Arg

```

207

```

          5          10          15
Cys Ser His Ile Arg Gly Pro Ile Lys Ile Ala Arg Asn Lys Phe Pro
          20          25          30
Arg Thr Leu Thr Ser Gln Glu Leu Arg Arg Phe Ala Glu Tyr Ser Gly
          35          40          45
Met Met Phe Gly Asp Gln Thr Thr Ala Gly Gln Lys
          50          55          60

```

<210> 584  
 <211> 76  
 <212> PRT  
 <213> Homo sapiens

```

<400> 584
Met Cys Leu Cys Ile Pro Leu Gly Gly Tyr Gln Glu Leu Cys His Cys
          5          10          15
Met Ser Thr Ser Asp Gly Phe Ala Pro Pro Pro Gln Leu Gly Ser Arg
          20          25          30
Cys Ser His Ile Arg Gly Pro Ile Lys Ile Ala Arg Asn Lys Phe Pro
          35          40          45
Arg Thr Leu Thr Ser Gln Glu Leu Arg Arg Phe Ala Glu Tyr Ser Gly
          50          55          60
Met Met Phe Gly Asp Gln Thr Thr Ala Gly Gln Lys
          65          70          75

```

<210> 585  
 <211> 50  
 <212> PRT  
 <213> Homo sapiens

```

<400> 585
Met Val Tyr Arg Phe Gly Gln Met Ser Asp Asn Pro Phe Tyr Ile Leu
          5          10          15
Ala Ser Leu Gly Ser Ser Ser Cys Arg Asn Gly Leu Ala Ser Lys Trp
          20          25          30
Arg Gln Ala Asp Pro Ser Asp Gly Tyr Met Glu Pro Cys Phe Gln Leu
          35          40          45
Leu Phe
          50

```

<210> 586  
 <211> 60  
 <212> PRT  
 <213> Homo sapiens

```

<400> 586
Met Leu Val His Ile Tyr Ser Cys Cys Gly Met Val Tyr Arg Phe Gly
          5          10          15
Gln Met Ser Asp Asn Pro Phe Tyr Ile Leu Ala Ser Leu Gly Ser Ser
          20          25          30
Ser Cys Arg Asn Gly Leu Ala Ser Lys Trp Arg Gln Ala Asp Pro Ser
          35          40          45
Asp Gly Tyr Met Glu Pro Cys Phe Gln Leu Leu Phe
          50          55          60

```

<210> 587  
 <211> 1408  
 <212> DNA



&lt;213&gt; Homo sapiens

&lt;400&gt; 587

```

ctggacactt tgcgagggct tttgctggct gctgctgctg cccgtcatgc tactcatcgt 60
agcccgcccc gtgaagctcg ctgctttccc tacctcctta agtgactgcc aaacgcccac 120
cggctggaat tgctctgggt atgatgacag agaaaatgat ctcttctctc gtgacaccaa 180
cacctgtaaa tttgatgggg aatgtttaag aattggagac actgtgactt gcgtctgtca 240
gttcaagtgc aacaatgact atgtgcctgt gtgtggctcc aatggggaga gctaccagaa 300
tgagtgttac ctgcgacagg ctgcatgcaa acagcagagt gagatacttg tgggtgcaga 360
aggatcatgt gccacagatg caggatcagg atctggagat ggagtccatg aaggctctgg 420
agaaactagt caaaaggaga catccacctg tgatatttgc cagtttggtg cagaatgtga 480
cgaagatgcc gaggatgtct ggtgtgtgtg taatatgtac tgttctcaaa ccaacttcaa 540
tccccctctg cttctgatg ggaaatctta tgataatgca tgccaaatca aagaagcatc 600
gtgtcagaaa caggagaaaa ttgaagtcat gtctttgggt cgatgtcaag ataacacaac 660
tacaactact aagtctgaag atgggcatta tgcaagaaca gattatgcag agaatgctaa 720
caaattagaa gaaagtgccg gagaacacca cataccttgt ccggaacatt acaatggcct 780
ctgcatgcat ggaagtgtg agcattctat caatatgcag gagccatctt gcagggtgtg 840
tgctggttat actggacaac actgtgaaaa aaaggactac agtgttctat acgttggttc 900
cgttctgtga cgatttcagt atgtcttaat cgcagctgtg attggaacaa ttcagattgc 960
tgtcatctgt gtggtggtcc tctgcatcac aaggaaatgc cccagaagca acagaattca 1020
cagacagaag caaaatacag ggcactacag ttcagacaat acaacaagag cgtccacgag 1080
gttaattctaa agggagcatg tttcacagtg gctggactac cgagagcttg gactacacaa 1140
tacagtatta tagacaaaag aataagacaa gagatctaca catgttgcct tgcatttgtg 1200
gtaatctaca ccaatgaaaa catgtactac agctatatat gattatgtat ggatatat 1260
gaaatagtat acattgtctt gatgtttttt ctgtaatgta aataaactat ttatatcaca 1320
caatawagtt ttttctttcc catgtatttg ttatatataa taaatactca gtgatgagaa 1380
aaaaaaaaa aaaaaaaaaa rwmgaccc 1408

```

&lt;210&gt; 588

&lt;211&gt; 81

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 588

```

Met Pro Gln Lys Gln Gln Asn Ser Gln Thr Glu Ala Lys Tyr Arg Ala
                    5                      10                      15
Leu Gln Phe Arg Gln Tyr Asn Lys Ser Val His Glu Val Asn Leu Lys
                    20                      25                      30
Gly Ala Cys Phe Thr Val Ala Gly Leu Pro Arg Ala Trp Thr Thr Gln
                    35                      40                      45
Tyr Ser Ile Ile Asp Lys Arg Ile Arg Gln Glu Ile Tyr Thr Cys Cys
                    50                      55                      60
Leu Ala Phe Val Val Ile Tyr Thr Asn Glu Asn Met Tyr Tyr Ser Tyr
                    65                      70                      75                      80
Ile

```

&lt;210&gt; 589

&lt;211&gt; 157

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 589

```

Met Thr Met Cys Leu Cys Val Ala Pro Met Gly Arg Ala Thr Arg Met
                    5                      10                      15
Ser Val Thr Cys Asp Arg Leu His Ala Asn Ser Arg Val Arg Tyr Leu
                    20                      25                      30
Trp Cys Gln Lys Asp His Val Pro Gln Met Gln Asp Gln Asp Leu Glu

```

209

```

      35      40      45
Met Glu Ser Met Lys Ala Leu Glu Lys Leu Val Lys Arg Arg His Pro
  50      55      60
Pro Val Ile Phe Ala Ser Leu Val Gln Asn Val Thr Lys Met Pro Arg
  65      70      75      80
Met Ser Gly Val Cys Val Ile Leu Thr Val Leu Lys Pro Thr Ser Ile
      85      90      95
Pro Ser Ala Leu Leu Met Gly Asn Leu Met Ile Met His Ala Lys Ser
      100      105      110
Lys Lys His Arg Val Arg Asn Arg Arg Lys Leu Lys Ser Cys Leu Trp
      115      120      125
Val Asp Val Lys Ile Thr Gln Leu Gln Leu Leu Ser Leu Lys Met Gly
      130      135      140
Ile Met Gln Glu Gln Ile Met Gln Arg Met Leu Thr Asn
      145      150      155

```

&lt;210&gt; 590

&lt;211&gt; 347

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 590

```

Met Leu Leu Ile Val Ala Arg Pro Val Lys Leu Ala Ala Phe Pro Thr
      5      10      15
Ser Leu Ser Asp Cys Gln Thr Pro Thr Gly Trp Asn Cys Ser Gly Tyr
      20      25      30
Asp Asp Arg Glu Asn Asp Leu Phe Leu Cys Asp Thr Asn Thr Cys Lys
      35      40      45
Phe Asp Gly Glu Cys Leu Arg Ile Gly Asp Thr Val Thr Cys Val Cys
      50      55      60
Gln Phe Lys Cys Asn Asn Asp Tyr Val Pro Val Cys Gly Ser Asn Gly
      65      70      75      80
Glu Ser Tyr Gln Asn Glu Cys Tyr Leu Arg Gln Ala Ala Cys Lys Gln
      85      90      95
Gln Ser Glu Ile Leu Val Val Ser Glu Gly Ser Cys Ala Thr Asp Ala
      100      105      110
Gly Ser Gly Ser Gly Asp Gly Val His Glu Gly Ser Gly Glu Thr Ser
      115      120      125
Gln Lys Glu Thr Ser Thr Cys Asp Ile Cys Gln Phe Gly Ala Glu Cys
      130      135      140
Asp Glu Asp Ala Glu Asp Val Trp Cys Val Cys Asn Ile Asp Cys Ser
      145      150      155      160
Gln Thr Asn Phe Asn Pro Leu Cys Ala Ser Asp Gly Lys Ser Tyr Asp
      165      170      175
Asn Ala Cys Gln Ile Lys Glu Ala Ser Cys Gln Lys Gln Glu Lys Ile
      180      185      190
Glu Val Met Ser Leu Gly Arg Cys Gln Asp Asn Thr Thr Thr Thr
      195      200      205
Lys Ser Glu Asp Gly His Tyr Ala Arg Thr Asp Tyr Ala Glu Asn Ala
      210      215      220
Asn Lys Leu Glu Glu Ser Ala Arg Glu His His Ile Pro Cys Pro Glu
      225      230      235      240
His Tyr Asn Gly Phe Cys Met His Gly Lys Cys Glu His Ser Ile Asn
      245      250      255
Met Gln Glu Pro Ser Cys Arg Cys Asp Ala Gly Tyr Thr Gly Gln His
      260      265      270
Cys Glu Lys Lys Asp Tyr Ser Val Leu Tyr Val Val Pro Gly Pro Val

```

210

```

      275              280              285
Arg Phe Gln Tyr Val Leu Ile Ala Ala Val Ile Gly Thr Ile Gln Ile
  290              295              300
Ala Val Ile Cys Val Val Val Leu Cys Ile Thr Arg Lys Cys Pro Arg
  305              310              315              320
Ser Asn Arg Ile His Arg Gln Lys Gln Asn Thr Gly His Tyr Ser Ser
      325              330              335
Asp Asn Thr Thr Arg Ala Ser Thr Arg Leu Ile
      340              345

```

<210> 591  
 <211> 565  
 <212> DNA  
 <213> Homo sapien

```

<400> 591
actaaagcaa atgaacaagc tgacttgcta gtatcatctg cattcattga agcacaagaa      60
cttcatgcct tgactcatgt aaatgcaata ggattaaaaa ataaatttga tatcacatgg      120
aaacagacaa aaaatattgt acaacattgc acccagtgtc agattctaca cctggccact      180
caggaagcaa gagttaatcc cagaggtcta tgcctaata tggtatggca aatggatgtc      240
atgcacgtac cttcatttgg aaaattgtca tttgtccatg tgacagttga tacttattca      300
catttcatat gggcaacctg ccagacagga gaaagtactt cccatgttaa aagacattta      360
ttatcttgtt ttctgtcat gggagttcca gaaaagttta aaacagacaa tgggccagg      420
tactgtagta aagcatttca aaaattotta aatcagtgga aaattacaca tacaatagga      480
attctctata attcccaagg acaggccata attgaaggaa ctaatagaac actcaaagct      540
caattgggta aacaaaaaaa aaaaaa                                565

```

<210> 592  
 <211> 188  
 <212> PRT  
 <213> Homo sapien

```

<400> 592
Thr Lys Ala Asn Glu Gln Ala Asp Leu Leu Val Ser Ser Ala Phe Ile
  1              5              10              15
Glu Ala Gln Glu Leu His Ala Leu Thr His Val Asn Ala Ile Gly Leu
      20              25              30
Lys Asn Lys Phe Asp Ile Thr Trp Lys Gln Thr Lys Asn Ile Val Gln
      35              40              45
His Cys Thr Gln Cys Gln Ile Leu His Leu Ala Thr Gln Glu Ala Arg
      50              55              60
Val Asn Pro Arg Gly Leu Cys Pro Asn Val Leu Trp Gln Met Asp Val
      65              70              75              80
Met His Val Pro Ser Phe Gly Lys Leu Ser Phe Val His Val Thr Val
      85              90              95
Asp Thr Tyr Ser His Phe Ile Trp Ala Thr Cys Gln Thr Gly Glu Ser
      100             105             110
Thr Ser His Val Lys Arg His Leu Leu Ser Cys Phe Pro Val Met Gly
      115             120             125
Val Pro Glu Lys Val Lys Thr Asp Asn Gly Pro Gly Tyr Cys Ser Lys
      130             135             140
Ala Phe Gln Lys Phe Leu Asn Gln Trp Lys Ile Thr His Thr Ile Gly
      145             150             155             160
Ile Leu Tyr Asn Ser Gln Gly Gln Ala Ile Ile Glu Gly Thr Asn Arg
      165             170             175
Thr Leu Lys Ala Gln Leu Val Lys Gln Lys Lys Lys
      180             185

```

211

<210> 593  
 <211> 271  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(271)  
 <223> n = A,T,C or G

<400> 593  
 actttatgtt cnagtgcana aancncctg gattgccacc ntactctcag ggctgtgant 60  
 tgtgcnccca nagcaacctg ggcacgcggg gacagggggg ccnacaattg agggagcggg 120  
 gtccctagct ggggtctata catgncnggg naagggcngc tgagtnccat nagcaaagga 180  
 nctagnatnt gcgggggtgc ggccctgggc taccctttna agcatccntn gatccactcc 240  
 angaancng gggtagncag gtttnccaac a 271

<210> 594  
 <211> 376  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(376)  
 <223> n = A,T,C or G

<400> 594  
 cctttggggg nggggggaac ctttaccatt gtnccccttt atttcatttg gttngggttc 60  
 gcgccctcnn gggccaacaa agttatcgtn nttgaagaga anattttttt ggnttngncc 120  
 cgattaagcg ncaaagtgtg agcaaaangc cgtgccactt gtggcgtagc tncgtcgggt 180  
 cgattcgacg acaaggcgtn gcgcgntanc gttagtctcn aatngaccn gtggcatgag 240  
 cccacgangg nttcgtgtcg tcacatggnc tctagacata acgcncncn ttttttncag 300  
 agggggnatgc cgccttagg gaggnagggg tggggacact agccaancca nantctnacc 360  
 ccattgaaga aaaggn 376

<210> 595  
 <211> 242  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(242)  
 <223> n = A,T,C or G

<400> 595  
 agnctgctgn tcgtnccctn tatgtggctt catnntgagg acaanagtng cactgaggct 60  
 tgngnatgcc aggcaaggnc aagctggctc aaaaagcatc caccacctc tgnaangggg 120  
 atgccangag cangtgcacc agtcccaact angagnccn ggcagtntac atcttcttcc 180  
 acccctnaaa ntttgngcta caangnccat ttttctttt ctcttaaggg ncnctnggct 240  
 tc 242

<210> 596  
 <211> 535  
 <212> DNA  
 <213> Homo sapien

212

<220>  
 <221> misc\_feature  
 <222> (1)...(535)  
 <223> n = A,T,C or G

<400> 596  
 accagttgga tactgctaaa nagatattta tgcagcctca tatgttaagt cgtatatattt 60  
 gaaagctttt taaatttttt ctttaagaag atttttagatg cttatcactg agtaccagag 120  
 ggatgtaggc tgatgccctt atcaacaaag tcagggactg tggcacacaa ggattgacta 180  
 ctgcagacac ggccacaatg ctacctctag agggcctgaa tccccctgcc ctctctgggtg 240  
 gggagaaggg ctggcagagc cattagcatg ggctccggcc aatcctggcc actttgacac 300  
 tcctggtgct gaccaggggt cctggaggaa gggatgagggt gggcagtaga gatgctcagg 360  
 gcagtggccc ctttccatcc acactggaac tatttcagta ttttaccacc aattcagcca 420  
 ttcccttggtg cgtggtctga acatcagccc tgcctcagggt ctgagtttcc cctttgtaaa 480  
 gggaaagctc tggattcagg gagtgatgaa gaggtcatca tggctctgag aattc 535

<210> 597  
 <211> 257  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(257)  
 <223> n = A,T,C or G

<400> 597  
 tttcnatacc caaaantacc ccatattang accanacatt tgcctnggaa aaattaccat 60  
 tntntaactt ttgggccacc tgagannaaa tgggtgtaat ncatgataag atggancagn 120  
 attnctotta agatnngatn agaccccggt tttcaogga catatccaag nacccaatag 180  
 gnaacaagcc acgggnggag tcacaaacat atattcttta ctctcataat ccgtnncaca 240  
 naactnttgn acttgac 257

<210> 598  
 <211> 222  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(222)  
 <223> n = A,T,C or G

<400> 598  
 nntggntacc gtcnaaactt nnccttggtac ccgagctcgg atccactagt ccagtgtggt 60  
 ggaattccat tgtgttgggc tataagctgt aatagtggag ncggtgctngg ttcattgcan 120  
 nagnccctcc gcanncacnc ttgnnacaac ctgtgagnag gcnataaatt attcacataa 180  
 tcatcactgc atgaanctga ctcaaacgca tccacntaca cc 222

<210> 599  
 <211> 238  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(238)

213

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 599

gcatgacatc	ancgatgtnt	ttggnnacct	ganattngct	aaaactngng	natgccgggn	60
atgnaggttt	ggtantgatc	tatgcactca	catctcatgg	ggacgtttca	tgtggagtgn	120
tcgacaangt	tgctgnannc	gagaagtgat	gatctcagtt	gaaaggggtca	tgtgaataca	180
cnttacactt	gaaaaagaag	cacattggga	atatcacgaa	acgnccacca	acatcctg	238

&lt;210&gt; 600

&lt;211&gt; 232

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(232)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 600

cgaactat	tt	agactaccta	ggaaaattat	tttagtatca	gaagaatatc	aggggtgtag	60
tactcatcag	agctaaatga	gagcgcttta	aaaatgttag	tttgtcttcc	gccatttcta		120
cagaaagctg	caatttcagg	ttttcaacct	aataggtgat	atttaanaaa	aaaaaaaaagc		180
aatcgcaaat	agccccactg	cttttacaaa	tcattttttc	cccaacacaa	tg		232

&lt;210&gt; 601

&lt;211&gt; 547

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(547)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 601

cattgtgttg	gggaaaaaat	gatttgtata	agcagtgggg	ctatttgcca	ttgctttttt	60
tttttcttaa	atatcaccta	ttaggttgaa	aacctgaaat	tgcagctttc	tgtagaaatg	120
gcggaagaca	aactaacatt	tttaaagcgc	tctcatttag	ctctgatgag	tactacacc	180
ctnatattct	tctgatacta	aaataatttt	cctagtgtag	tctaaacttt	tttaaaaaga	240
catgtaatcc	gcggagttag	taactcaaaa	cgagtgcac	tnggaagtat	cgcagccgtt	300
nctggatnaa	attcccagct	tgctngcttg	ctnagccggg	gggcggtnaa	aaaaacatct	360
gcagcccngg	ggnaaaaacc	ttcgattgt	tcttacgtgt	ttacgttatt	ttatttccct	420
nnagcaaggc	nggganttgg	ggactcgaaa	tggtacagtt	gggctgggga	tcgcccttgt	480
tacataaaag	ncgtccagaa	gagggacggt	tacaggcngg	ganctccaaa	ggtcagtccc	540
tgccatt						547

&lt;210&gt; 602

&lt;211&gt; 826

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(826)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 602

cggggggnnt	tacgtctctc	tgacgctttt	tattgtacca	gggcgatccc	agcccaactg	60
------------	------------	------------	------------	------------	------------	----

214

taccattcga	gtccctactc	ctgccttgct	ctagggaaat	aaaataacgt	aaacacgtaa	120
gaacaatgcg	aaagcggttt	cttccttagg	ctgcagattg	tcttcttcac	cgccctgct	180
tagctagcta	gctagctggg	aatttaatcc	agaaacggct	tgcgatacct	cctagatgca	240
ctcgttttga	gttacaaact	ccgcggatta	catgtctttt	taaaaaagtt	tagactacac	300
tagggaaaat	tatttttagta	tcagaagaat	atcagggggt	gtagtactca	tcagagctna	360
atgagagcgc	tttaaaaatg	ttagtttgct	ttccgccatt	tctacagaaa	gctgcaattt	420
caggttttca	ncctaatagg	tgatatntaa	gaaaaaaaaa	acaatcgcan	atagcccaact	480
gctttttcaa	atcatttttc	tcttctagggt	atagcctgtc	aggtggccta	atgtattttt	540
gacatctcta	ggaattttta	tagaccagaa	atgggtgccca	gagatatgcc	tgactaatc	600
ttaagtgggg	atttatgtat	ttctcaanca	agtgattaaa	gcaaaactag	gcacgaatga	660
aatcaagatc	tttaggccag	aaatcatgaa	nanttttana	attattttan	gaatctgtgg	720
cttctcttct	taaaatngaa	aaaaaaattg	tttaaaccca	naaggtctga	ataccaagc	780
nccctgaacn	anagaacaan	gccggagcac	cccctcccaa	atcccc		826

<210> 603  
 <211> 817  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(817)  
 <223> n = A,T,C or G

<400> 603						
nnangacttt	tgtggtntta	tacaattntt	ttttctattt	ctatgaagag	aaagccacag	60
agtccataaaa	taattctaaa	actcatcatg	actttcttgc	ctaaaaagatc	ttgatttcaa	120
tcgtgcctag	ttttgcttta	atcacttgct	tgagaaatac	ataaatcccc	acttaagatt	180
agtgcaggca	tatctctggc	acccatttct	ggttctatta	aaattcctag	agatgtcaaa	240
aattacatta	ggccacctga	caggctatac	ctagaagaga	aaaaatgatt	tgtaaaagca	300
gtggggctat	ttgcgattgc	tttttttttt	tcttaaatat	cacctattag	gttgaaaacc	360
tgaatttgca	gctttctgta	gaaatggcgg	aagacaaact	aacattttta	aagcgctctc	420
atttagctct	gatgagtact	acaccctga	tattctctg	atactaaaat	aattttccta	480
gtgtagtcta	aactttttta	aaaagacatg	taatccgcgg	agtttgtaac	tcaaaacgag	540
tgcatctagg	aggtagcgca	agccgtttct	ggattaaatt	cccagctagc	ttgcttgctt	600
agcaggggcg	ggnaaanaag	acatctgcag	cctagggaag	aaaacctttc	gcattgttct	660
tacgtgttta	cgttatttta	tttctanaaa	caaggcngaa	ttgggactcg	aatggttcag	720
ttgggggtgg	ggatccctcg	gtncataaaa	ngtcanaaag	anggtacagg	cggaacncca	780
agggtcgtcc	tgcatttana	ctcggaattt	tgggtgcc			817

<210> 604  
 <211> 694  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(694)  
 <223> n = A,T,C or G

<400> 604						
cttttcaaat	catttttinct	cttctaggta	tancctgtca	ggtggcctaa	tgtaattttt	60
gacatctcta	ngaattttta	tagaaccaga	aatgggtgcc	agagatatgc	ctgcactaat	120
cttaagtggg	gatttatgta	tttctcaagc	aagtgattaa	agcaaaacta	ggcagcattg	180
aatcaagat	cttttaggca	anaaagtcac	gatgagtttt	agaattattt	taggactctg	240
tggtctttct	ttcatagaaa	tagaaaaaaa	aattgtataa	aaccacaaaa	ggtcctgaat	300
agccaaagca	acactganca	aaaagaacan	agcagggaag	caacacacta	ccngaattca	360
aattatacta	ccagggtgta	gtaaccaaaa	cagcattcta	ttggcataaa	atagacacca	420

## 215

agaccaatg	ancagaataa	agaacccccac	aaataaatcc	atatatntac	cgccanctga	480
ttatcaataa	cnaacaccaa	gaacatatnt	taagggaent	nctattcaat	aantagtgct	540
ggnaaaaaact	gggaaatcca	tatgcagaaa	naatgaaact	agaccctat	ccctcaccat	600
acgcaaannt	caacttcgga	atgggattac	aaaacttaag	acattccaac	ccaagaaact	660
atnaaancta	ctattaagaa	aacagatcnc	nccc			694

&lt;210&gt; 605

&lt;211&gt; 678

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(678)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 605

taaaaatcta	gactacacta	ggaaattatt	ttantatcag	aagaatatca	ggggtgtagt	60
actcatcana	gctaaatgag	agcgctttta	aaatggttagt	ttgtcttccg	ccatttctac	120
agaaagctgc	aatttcaggt	tttcaacctt	ataggtgata	tttaagaaaa	aaaaaaagca	180
atcgcaaata	gccccactgc	ttttacaaat	catTTTTTct	cttctaggta	tagcctgtca	240
ggtggcctaa	tgtaattttt	gacatctcta	ggaattttta	tagaaccaga	aatgggtgcc	300
agagatatgc	ctgcactaat	cttaagtggg	gatttatgta	tttctcaagc	aagtgattaa	360
agcaaaaacta	ggcacgattg	aaatcaanat	cttttaggca	agaaagtcac	gatgagtttt	420
anaattattt	taggactctg	tggttttctc	ttcatagaaa	tagaaaaaaa	aaattgtata	480
aaaaccacaa	aaggctcctga	atagcccaaa	gcaacactga	acaaaangaa	caaagcagga	540
agcaacacac	taccggaatt	caattatact	accaaggtgt	antaaccaaa	acagcattct	600
attgggcata	aaatagacca	aagaccagtg	ggaaacagaa	taaagaancc	caaaataaat	660
cctatatatta	cngcccnc					678

&lt;210&gt; 606

&lt;211&gt; 263

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(263)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 606

gtggggctcng	cancagccaa	ctcagcttcc	tttcgggctt	tgtagcaga	cggatcatcc	60
tctagtccac	tgtgntcaaa	ttccattgtg	tgggggccnc	tcgcctcggc	canagatctg	120
agtgancana	cntgtcccca	ctgaggtgcc	ccacagcngn	ttgtnttcag	cangggctna	180
caactcgacc	ggcagcgnan	ggctggcaga	antgngcgcc	tnnctcattc	ctacgcngtn	240
ngccgcagga	aggangacag	gcc				263

&lt;210&gt; 607

&lt;211&gt; 22

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Primer

&lt;400&gt; 607

ccatgtgggt cccggttgtc tt

22



216

<210> 608  
<211> 22  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Primer

<400> 608  
gataggggtg ctcaggggtt gg

22

<210> 609  
<211> 40  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Primer

<400> 609  
gctggacagg gggcaaaagc tggggcagtg aaccatgtgc

40

<210> 610  
<211> 27  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Primer

<400> 610  
ccttgtccag atagcccagt agctgac

27

<210> 611  
<211> 46  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Primer

<400> 611  
gatagagaaa accgtccagg ccagtattgt gggaggctgg gagtgc

46

<210> 612  
<211> 40  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Primer

<400> 612  
gcacatgggt cactgcccc a gcttttgccc cctgtccagc

40

<210> 613  
<211> 38  
<212> DNA

217

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Primer

&lt;400&gt; 613

gccgctcgag ttagaattcg gggttggcca cgatgggtg

38

&lt;210&gt; 614

&lt;211&gt; 53

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Primer

&lt;400&gt; 614

cggcgggcat atgcatcacc atcaccatca catcataaac ggcgaggact gca

53

&lt;210&gt; 615

&lt;211&gt; 46

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Primer

&lt;400&gt; 615

gcactcccag cctcaccacaa tactggcctg gacggttttc tctatc

46

&lt;210&gt; 616

&lt;211&gt; 1350

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 616

atgcatcacc atcaccatca catcataaac ggcgaggact gcagcccgca ctgcagccc	60
tggcaggcgg cactggtcat ggaaaacgaa ttgttctgct cgggcgtcct ggtgcatccg	120
cagtgggtgc tgtcagccgc aactgtttc cagaactcct acaccatcgg gctgggcctg	180
cacagtcttg aggcgacca agagccaggg agccagatgg tggaggccag cctctccgta	240
cggcaccag agtacaacag acccttgctc gctaaccgacc tcatgctcat caagttggac	300
gaatccgtgt ccgagtctga caccatccgg agcatcagca ttgcttcgca gtgccctacc	360
gcggggaact cttgcctcgt ttctggctgg ggtctgctgg cgaacggcag aatgcctacc	420
gtgctgcagt gcgtgaacgt gtcggtggtg tctgaggagg tctgcagtaa gctctatgac	480
ccgctgtacc accccagcat gttctgcgcc ggcggagggc aagaccagaa ggactcctgc	540
aacggtgact ctggggggcc cctgatctgc aacgggtact tgcagggcct tgtgtctttc	600
ggaaaagccc cgtgtggcca agttggcgtg ccagggtgtc acaccaacct ctgcaaattc	660
actgagtgga tagagaaaac cgtccaggcc agtattgtgg gaggctggga gtgcgagaag	720
cattcccaac cctggcagggt gcttgtggcc tctcgtggca gggcagctcg cggcggtgtt	780
ctggtgcacc cccagtggtt cctcacagct gccactgca tcaggaacaa aagcgtgatc	840
ttgctgggtc ggcacagcct gtttcatcct gaagacacag gccaggattt tcaggtcagc	900
cacagcttcc cacaccgct ctacgatatg agcctcctga agaatcgatt cctcaggcca	960
ggtgatgact ccagccacga cctcatgctg ctccgcctgt cagagcctgc cgagctcacg	1020
gatgctgtga aggtcatyga cctgcccacc caggagccag cactggggac cacctgctac	1080
gcctcaggct ggggcagcat tgaaccagag gagttcttga ccccaaagaa acttcagtgt	1140
gtggacctcc atgttatttc caatgacgtg tgtgcgcaag ttcaccctca gaaggtagcc	1200
aagttcatgc tgtgtgctgg acgctggaca gggggcaaaa gctggggcag tgaacctgt	1260
gccctgcccg aaaggccttc cctgtacacc aagggtggtc attaccggaa gtggatcaag	1320

218

gacaccatcg tggccaaccc cgaattctaa

1350

&lt;210&gt; 617

&lt;211&gt; 449

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 617

Met	His	His	His	His	His	His	Ile	Ile	Asn	Gly	Glu	Asp	Cys	Ser	Pro
1				5					10					15	
His	Ser	Gln	Pro	Trp	Gln	Ala	Ala	Leu	Val	Met	Glu	Asn	Glu	Leu	Phe
			20					25					30		
Cys	Ser	Gly	Val	Leu	Val	His	Pro	Gln	Trp	Val	Leu	Ser	Ala	Ala	His
		35					40					45			
Cys	Phe	Gln	Asn	Ser	Tyr	Thr	Ile	Gly	Leu	Gly	Leu	His	Ser	Leu	Glu
	50					55					60				
Ala	Asp	Gln	Glu	Pro	Gly	Ser	Gln	Met	Val	Glu	Ala	Ser	Leu	Ser	Val
65					70					75					80
Arg	His	Pro	Glu	Tyr	Asn	Arg	Pro	Leu	Leu	Ala	Asn	Asp	Leu	Met	Leu
				85					90					95	
Ile	Lys	Leu	Asp	Glu	Ser	Val	Ser	Glu	Ser	Asp	Thr	Ile	Arg	Ser	Ile
			100					105					110		
Ser	Ile	Ala	Ser	Gln	Cys	Pro	Thr	Ala	Gly	Asn	Ser	Cys	Leu	Val	Ser
		115					120					125			
Gly	Trp	Gly	Leu	Leu	Ala	Asn	Gly	Arg	Met	Pro	Thr	Val	Leu	Gln	Cys
	130					135					140				
Val	Asn	Val	Ser	Val	Val	Ser	Glu	Glu	Val	Cys	Ser	Lys	Leu	Tyr	Asp
145					150					155					160
Pro	Leu	Tyr	His	Pro	Ser	Met	Phe	Cys	Ala	Gly	Gly	Gly	Gln	Asp	Gln
				165					170					175	
Lys	Asp	Ser	Cys	Asn	Gly	Asp	Ser	Gly	Gly	Pro	Leu	Ile	Cys	Asn	Gly
			180					185					190		
Tyr	Leu	Gln	Gly	Leu	Val	Ser	Phe	Gly	Lys	Ala	Pro	Cys	Gly	Gln	Val
		195					200					205			
Gly	Val	Pro	Gly	Val	Tyr	Thr	Asn	Leu	Cys	Lys	Phe	Thr	Glu	Trp	Ile
	210					215					220				
Glu	Lys	Thr	Val	Gln	Ala	Ser	Ile	Val	Gly	Gly	Trp	Glu	Cys	Glu	Lys
225					230					235					240
His	Ser	Gln	Pro	Trp	Gln	Val	Leu	Val	Ala	Ser	Arg	Gly	Arg	Ala	Val
				245					250					255	
Cys	Gly	Gly	Val	Leu	Val	His	Pro	Gln	Trp	Val	Leu	Thr	Ala	Ala	His
			260					265					270		
Cys	Ile	Arg	Asn	Lys	Ser	Val	Ile	Leu	Leu	Gly	Arg	His	Ser	Leu	Phe
		275					280					285			
His	Pro	Glu	Asp	Thr	Gly	Gln	Val	Phe	Gln	Val	Ser	His	Ser	Phe	Pro
	290					295					300				
His	Pro	Leu	Tyr	Asp	Met	Ser	Leu	Leu	Lys	Asn	Arg	Phe	Leu	Arg	Pro
305					310					315					320
Gly	Asp	Asp	Ser	Ser	His	Asp	Leu	Met	Leu	Leu	Arg	Leu	Ser	Glu	Pro
				325					330					335	
Ala	Glu	Leu	Thr	Asp	Ala	Val	Lys	Val	Met	Asp	Leu	Pro	Thr	Gln	Glu
			340					345					350		
Pro	Ala	Leu	Gly	Thr	Thr	Cys	Tyr	Ala	Ser	Gly	Trp	Gly	Ser	Ile	Glu
		355					360					365			
Pro	Glu	Glu	Phe	Leu	Thr	Pro	Lys	Lys	Leu	Gln	Cys	Val	Asp	Leu	His
	370					375					380				
Val	Ile	Ser	Asn	Asp	Val	Cys	Ala	Gln	Val	His	Pro	Gln	Lys	Val	Thr
385					390					395					400

219

Lys Phe Met Leu Cys Ala Gly Arg Trp Thr Gly Gly Lys Ser Trp Gly  
                                   405                                  410                                  415  
 Ser Glu Pro Cys Ala Leu Pro Glu Arg Pro Ser Leu Tyr Thr Lys Val  
                                   420                                  425                                  430  
 Val His Tyr Arg Lys Trp Ile Lys Asp Thr Ile Val Ala Asn Pro Glu  
                                   435                                  440                                  445  
 Phe

<210> 618  
 <211> 385  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(385)  
 <223> n = A,T,C or G

<400> 618  
 ctgtgctgag aaccaaagc tatgancact gcttttccaa atgtccataa naccaacatt 60  
 tttatcacta ccaccatcac ctgggagctc nttagaaagc tagtctcccg ggcaccaccc 120  
 tggcctactg aacctaagt gcatttaaca agattnacgt ngaaatctgc aaagcacagg 180  
 ggcngataac agtaccacct gntctggttc ctanccccc gacccttaca gtctaactgg 240  
 gacacaaggg cttnaaatca aattgcctat cattaagata tacaanganc ntgagaaact 300  
 gctncactta tntattaagg ngctctaaga cttagaaacn aaangcantg ctgagangat 360  
 tcaaatatga ngggggnac tttnc 385

<210> 619  
 <211> 869  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(869)  
 <223> n = A,T,C or G

<400> 619  
 gatatcccgg gaattcgcgg ccgcgtcgac ctctacttgt ttagacataa atgcagtcta 60  
 gcattaaaaga tccttttaaaa aaatgttttc ccaatgggta aaagacaagc toaaataaat 120  
 gaactctcat acatatgcca aaattgatga gtagataaat atttcagtag gtagttacta 180  
 gctttctgtg tatgagttaa catatgggag aaatttaaaa cactaaagta gactcaatga 240  
 aagcatagta tcctatgtat tcgtttttca gaaatgtcta atgaaggaag gaaacaatga 300  
 atgaatgcc ttattcctct tagagtgttg ggacatgggt ttgcctgaaa acttcatgtg 360  
 aattttatat tttgctacac attacacca tottagactt atacgtataa gacataaggc 420  
 atatcttatg tcttacatgt ataataatct aagcagaaca aaaaataacg aaatattttc 480  
 ttcccaaat ttttagaca gatggatttt ccggaagat gtgttttagct tttaatcctg 540  
 tgggtttgtg taccacctgg cactacagag tgttgctcta attcagtgag ttgtaactct 600  
 ggggtgaacag tggaaatact aggggtacatt ttaaaaatgc taatgctcgg gcctcgctga 660  
 agaccaaatt aattggaatc totgngggng gnattgatct ttttataatc tttctanang 720  
 attctaattg gcttccagg atgaaaacn ctgntggagc tnggaacctt ccttttagttt 780  
 ggagaaaacc cgatgagggt ntnttaggcn ccgcctnttt ttggcctggg ctccccccct 840  
 tatntntntt tgggaangnc cnaattttt 869

<210> 620  
 <211> 339  
 <212> DNA

220

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(339)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 620

gngcgggctt	cnccgtgctt	gctctcgctg	ccgacgctct	ttttccacca	gctgtaggan	60
aagcccgaag	accactgggc	ccccgggtag	cccaggtacc	actggtcctc	ctggctcctg	120
acgctnoggg	tcttcctcgt	ggcgtagact	gccagcttgc	gagacccctc	agccccctcc	180
cgcttttctc	caccccagga	ggccatcagt	agcgagctac	tgccctgggc	acaacctccc	240
agcangatat	cccgcgggtt	ccaatctgcg	aaaggaggac	cgccnagccc	gaaatgccna	300
gccagcgnat	cactgccacg	ccgagccnag	cgctcgtgc			339

&lt;210&gt; 621

&lt;211&gt; 267

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(267)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 621

gggngcgtg	gtcccnggta	gccaaagtaca	tggtcctcct	ggctcctgac	gctacgggtc	60
ttcctcgttg	cgtagactgc	cagcttcgga	gaccctcag	cccctcccgc	cttttctcca	120
ccccaggagg	ccatcagtag	cgagctactg	cctcgccac	aacctcccag	caggatngcc	180
cgcggtttcc	aatctgcgaa	aggaggaccg	ccnagccaga	aatgccnagc	cnagcgatca	240
ctgccacgcc	nagccnagcg	ctcgtgc				267

&lt;210&gt; 622

&lt;211&gt; 847

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(847)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 622

cttangntgt	cgactgacgt	catgcatgan	ttaaagcaga	ggtttggtga	aatttatgaa	60
aaatacaaaa	ttccggcttg	tcctgaggaa	gagccactac	ttgataactc	tacaagagga	120
acagatgtga	aggatattcc	ctttaatttg	acaataaaca	tacctggttg	tgaggagaa	180
gatgcatctg	aaatatctgt	ctcagtggta	ttcgagacat	ttcctgaaca	aaaagaacct	240
agtcctcaaaa	atatcatcca	tccatactat	catccgtact	ctgggtccca	ggaacatgtt	300
tgccagtcac	cttctaagct	tcattttacat	gaaaataaat	tagactgcga	caatgataac	360
aaactaggca	ttggacatat	ttttagtaca	gataacaact	ttcataatga	tgcaagcact	420
aagaaagcaa	ggaaccacga	agtggttacg	gttgaaatga	aagaagacca	agagtttgat	480
ttgcaaatga	caaaaaatat	gaacaaaaat	agtgcagtg	gcagtacaaa	taactataaa	540
agcctgaaac	ctaaattaga	aaatctgagt	tctttaccac	cagattctga	cagaacatca	600
ggaagtatat	ctacatgaag	aattacagca	agacatgcc	aaagttaaag	aatgangtca	660
acacattaga	aanaagantt	ctgggctttg	aagaaagaaa	atgttccact	tcataaagaa	720
ggttgaaaga	agaatgggag	agccngaana	ttttggccn	gaaattttcg	ggaaccctac	780
tggtatgggtc	nactggttgg	ccatgaatga	ataatggact	aatcnccaa	ttcctnggga	840
agggaat						847

221

<210> 623  
 <211> 681  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(681)  
 <223> n = A,T,C or G

<400> 623  
 aaaactgtac tcgcgcgctg catgtcgaca ctagtggatc caaagaatcg gcacgagcga 60  
 aaangctcan gcagcccgcc tggccgcgcg cgctcctccc ccaggaag ccaangtggg 120  
 ngctgatgtg gctgcangag ctcttttcac agccctcan gtgganctgg ttgggcccgcg 180  
 gctgccangg gcggaagtgg gtgtccccc gtctcagccc caaggctgcc cctcacaag 240  
 cactggtggt ttgcctccac tgccaccttg ggctccgaac ccgctcccct gctgtggang 300  
 cccaccgtgg gaatccaggt cccaggtgg actgcctgcc ttgccctcac tgcccactct 360  
 gccacactt ccctgcctag anaccgggaa ggggctgtgt cgggtantgg gccacctgg 420  
 atgtggcagc accgactgtg ggggtggacc tggccttgcc gggtgcaaaa gtgggggccc 480  
 ngggaaaagc acctgaagtg gccctgaaaa atccccctt aatttttccc caatttggg 540  
 ctcaacaaa aggaatttgc tgaagccaan ggtaccaagg tcaccctaa ggccagggtg 600  
 aaaaggtccc aaaattccaa tccccacct ttgggcttnc ctcttggaac ccgggcccc 660  
 tctcntgaan ttttaaaaaa n 681

<210> 624  
 <211> 661  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(661)  
 <223> n = A,T,C or G

<400> 624  
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 tttttttttt tctctttctg actgtccatg gacaaatgaa actaacttaa tctaactaaa 120  
 aaacacaact atattttgaa gattttetat ctgcactcaa ggacacttcc cacnccgttg 180  
 ttgttacctt ttggctctgt ctctgaacat gaaattnatc tcaagggtt ngatttctgg 240  
 acctcctatt cctgtctatg gttgatatt tcttgggctc cagggccact gttgcattgg 300  
 gntgacagnt acctcctagc ccatancctc ctatcttggg aaacaaacct aacaactacg 360  
 tgtaccttcc atagatctct gattgagttc cagtatnccg ttgctcatgg gcgattcact 420  
 tgaatccgtt attggtgcca acaatcctga ctcatggggnn aatggatcct atcacgttcc 480  
 cctgattngc aacccttgta tacatanatc taatcgcata gaatctagn tnggntatgc 540  
 gcggctacgc tatcagggtt tgntaactat ngcatggcta cgaancctga tcatgatcna 600  
 gggctcatga ctcttatcag gggggttggg ccngcttct ttttcnnacc ttggtaaaaa 660  
 c 661

<210> 625  
 <211> 181  
 <212> DNA  
 <213> Homo sapien

<400> 625  
 gcaacaatca gatcatgtta aagtaaatct ccattgccct ggatcacttc aggatttaat 60  
 tgtccaagga gaggagggtt ctctgtgtaa aaaaagggtg ggaaatgttt gagagtaaaa 120  
 aatacaaaat tcaaccggtc gaaaatacac cactccatto agtgccttac ccccataagc 180

222

c 181

<210> 626  
 <211> 181  
 <212> DNA  
 <213> Homo sapien

<400> 626  
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 tgtccaagga gagcaggggtt ctctgtgaa aaaaagggtg ggaaatgttt gagagtaaaa 120  
 aatacaaaat tcaaccggtc gaaaatacac cactccattc agtgctctac ccccataagc 180  
 c 181

<210> 627  
 <211> 813  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(813)  
 <223> n = A,T,C or G

<400> 627  
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 gtgagcagag gagaacttgc gatggcaaag ttaaaaacaa gaggagatga tggctttggt 120  
 gtggcacagg atgttaaaaa aattctcctg tccttaagga gttactgcta tttgagtaat 180  
 gtgccacttc cctacatagc cttctatgca gaaatgctat atttccactt cacaaccag 240  
 aacgtgcatt ttattttaca tttagaggag gaacaaacaa ccagaaggca aaaactggtg 300  
 cattattttt tgcaattctc ttggaaagag ttcgttttta acttctgctc agacagcaca 360  
 caactactgg gaatatatatt taatttcaaa tctgatgtgt gacatctggt aactcattta 420  
 ttgctaataga agttttcaca ggaagcagca gtcaccagta gtcctctta tttttcagtt 480  
 ggcaaaagtgt tgtttacctt ttattggcct gcatcgggtg ctcttatcac aggatattta 540  
 attagaaaac gcaagtagcc taacatagaa nagaatgggà gtggtagata atagtagata 600  
 gaatggctaa atatttttat tacagtgatg taatatcact gnaatttatg gttaaaaatt 660  
 atgtaatact caaaaggaat tctcagactg gcgaaacagc tggnaacag ctntcacagg 720  
 gctttanact cctnttgagc tttcccctg ntggacttta gtcttccttt taencccgna 780  
 gtnccattn nttaccaatt gtnccgggaa ana 813

<210> 628  
 <211> 646  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(646)  
 <223> n = A,T,C or G

<400> 628  
 tttggngngn ggtgtctcnt ttgggtggac tttttgggtc gtagggcccc aaggccgtta 60  
 atcccgtaat aacggaagac gaagaagagt cagaagagtg cttctataag gatcgggacg 120  
 agactacctt agaggaataa aggaaaaaag cagaggagga agagtgttag aaggagttag 180  
 aagaacacca cagtcggttc tgaacctgga gccttatcaa aaaggtctag ataaacgata 240  
 gcgatctcga tatcgagctc aagaggtagg tttagagact tctcgtcctc gagagcgaaa 300  
 tggaagatct cgacgacgat aagaagttaa agtgtagagg gtgcttgagg agcgcggtga 360  
 aggattctgc ggagggaccc atcgacgtag agacttgaag gcctactaag gtccacaaga 420  
 agcccggctc tttctccgaa tggctcgagc gtacagtatg cgacgtcgat cggcagacaa 480

223

gctggcggtgta	gactcgaagt	gttcggggcga	atcgacttat	aatagtcgcg	cgctagtaac	540
gtaggaacac	gaagagtagt	cgaaagaaaa	cgtttagtga	gggaaaagat	tagggaaaaa	600
ggagaggctt	aataactaag	acacttggag	cctaggccaa	cgcgaa		646

&lt;210&gt; 629

&lt;211&gt; 617

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(617)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 629

gccccnccc	ccctcctnng	gcttatnngg	acagaccac	gtagtactct	aaatcttctc	60
ctacgccgga	caacggaccc	tataccaatt	cgaatcttgg	acactccgac	cgccggattc	120
tcttcccctt	tcggcttccc	ctttctgtcg	gtacccctcc	ctagtcgtct	cctacacctt	180
cgtaccgtcg	atatatagtc	gocgcggact	agcctattta	ggtgtcctag	actcgttatt	240
gatccactca	ttagtctagt	actatgcgtc	acgtatctta	gttgccctaag	agggagatta	300
aatcctccac	aagttccgac	gaattcctgg	actctcgtac	tagcaaaactt	tcttatgagg	360
cttccttgta	tatcttctgg	atgtttctcg	tgtcccggtc	ctccgctact	actagagctc	420
cttgccctat	ctctagaagt	agaggactct	cgggttcggt	ctccaaatct	agcgctagag	480
ctatcgctac	ccgctcgatt	cccccagcgg	aatcttgaaa	cctgaggtag	tacacaaacc	540
ctcncatct	tccctcgggt	gtccttctt	ctcatccccc	cttcccgcct	tctcgggaan	600
gaatctactt	tancttc					617

&lt;210&gt; 630

&lt;211&gt; 644

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(644)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 630

cnntcggcnt	gggttttntt	ctgagnnncc	ccccccccc	ccccccaaa	cttacacca	60
ccaaacactt	tccgcccct	acctaggaga	cattagaagg	gtttaggctt	cggcgtatag	120
taaagtccct	tacctcgga	gtagagaatt	cggtatttaa	attcagggtt	agaggctcgc	180
tcgttagatt	tatagttag	gtttagaatc	ggaaaccttc	gatcttcctt	agaagggtaa	240
taagtgaggc	cctaaatccg	tctaaccaag	gcgttaaggt	ccgtacctaa	acctagtctt	300
atcttctatc	aggcgcacca	atataggtag	gttctacttt	cgtataggcc	ttaaggaata	360
gttcggtagt	tatcgaaggc	actcctctct	aggctaggct	tttctcagtc	ttagtactcc	420
gggaccgtcg	tcgcanaaat	atcgatggac	ggtaggtatc	tccgcgttac	gcgtcgggct	480
agggatatag	agcgaattat	cggcgagagg	cggtcgctan	gaatcgggtat	caatatgntg	540
ttctttaccc	tacggatatc	ggcagaaaac	ataaaacctt	ctnaccangg	ataagggtat	600
atcggacccc	taaaataaca	gtaacattta	gantactagt	accc		644

&lt;210&gt; 631

&lt;211&gt; 526

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(526)



224

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 631

centcggtt	gggtttttt	ctgagcccc	ccccccccc	ccccccccc	cccccccggc	60
cccatagccc	caccggnccc	acccaaattt	taacaaaata	aatntaccta	tcgntcacct	120
atcccnegta	tcgngtaggt	cggtagccgt	accgngatc	ncnacgattn	ttcgggtcgt	180
cncccttaan	acggnccggt	agccnccgga	anaaatacta	cgagngactc	taatntagca	240
anaccgcg	tcnattanta	gcatccttag	tcttccaatg	ncgnggattn	ngaatacctn	300
naagttagcg	ggtagaacgg	gtcccggtcc	cccgccctct	tttcaattaa	cgccgggtac	360
aaantcggtt	tctaaattcc	ncacgaattt	ngncggcaac	attcncgggn	ccttattanc	420
cntttccaac	cccgatacnc	nagctcgatc	gggctttanc	gaatccgggg	tcnccccga	480
ngantccggg	tcctttgagt	ngctctagga	cggttacgac	ggagga		526

&lt;210&gt; 632

&lt;211&gt; 647

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(647)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 632

tttggngg	ggngctcat	ttgggtggac	tttttgggtc	gtaggaacct	ggtatgaggg	60
gtgttttgag	tttcttcttc	gtcgtctctg	ggaggttcgg	tttcgattga	gattcgggtt	120
cgtctttatc	ttacgaggca	ccctgatatt	gttgcgtttt	ggtttggttg	tggagagttt	180
tgtcctactc	tagcgggtca	tgccgatgat	atgtagccctg	cgtggcctga	tagtgatggt	240
gtgagcttga	gaggggagtt	gtgggtgttg	cgggcggagt	aggagggggt	ggagcaccgg	300
gattgggaga	tatagaatca	taagtgttag	gtataggtcg	attgagcgag	ttcgtggaat	360
tcgtgtggtc	atcataatta	gagtgaggat	gggctctata	tttcttagag	gacgcacggt	420
cgtgattcgg	ggtttgatgg	gtgttctctc	tgtgggcacg	attagcttgt	tcatgatggt	480
aaggaccata	ctgtttcgaa	tgaggattcg	tgtcttcgga	ttgttgtgga	tattgtggnc	540
tanactat	agtgtaaacc	ggaggtgggt	tgcctgtgtg	gagtatccga	nnttcattcg	600
ganggtatgc	gtgcggagcg	gtccttgtag	acattccgga	aaaatgg		647

&lt;210&gt; 633

&lt;211&gt; 630

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(630)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 633

tccttcggct	tgggtttttt	tctgaccccc	ccccccccc	ccccctcgga	aggcctctag	60
gtccaccacc	gtctctctaa	tcctcaggaa	ccgatccacc	caaccaactt	actaatgtcc	120
tacagtaa	accogagaat	ataaaccac	acctaggcct	ccaatcctac	cagggagca	180
agaagccgta	gtctagcgta	ttacgaaccc	gagatagaga	cggagatact	tagttttatt	240
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tggcggatat	gggggcgggt	cgtctcttta	ttcttctata	ccacgtcaat	aggaaatgtag	360
atatacctag	atgttcccg	agaaagagac	gttagaggtc	tccgaagcta	taaaggagag	420
gcgcgaagaa	acttcgtact	ctagctttat	ataggtagtc	gctctagtcc	cataagcgac	480
gagagatcta	ctagatttctg	gtatcgccgt	cgtatgtatt	cgaaatagtc	ttcttcccct	540
tttcgatctc	ctctctatac	tacatggnga	ttatagtcnt	aagatagtc	ggatattagg	600
atattagtta	tatgacgttc	gacgggacgg				630

225

<210> 634  
 <211> 647  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(647)  
 <223> n = A,T,C or G

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<400> 634
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caaccctata gtttactcgt ataggggaat cgaggagaaa taggaacgaa gagcgggtga      120
taaagagaaa gtacttttct ttatatgtta agagcttagc gtaatgactt tcgttatatg      180
gctagttagt tttatccggc gttatagggc ttagttctgg ttatctcggg tctaattccc      240
ttagtatgct cgggagttta acgaggtcac gggatagcgc gtaccctttc taaggttctt      300
ggaaagctat tcgttattta tcgcgattct cgaggtcgaa aggatcaagg atcttccctt      360
ttactaccct agtcgggtta gcggtcggtc aaaactagt tagtaccttt acctcctcga      420
aagttatagt cgaaacaacg tattagtcga aattatagcg gatagatcga gacggttctt      480
tctcgggttc tcagccggta atccctctat ttgggggtct tctccctctt cccctttgtc      540
ttccgcctta gcttccaagg ttccctcgaa gcgaggggtt ctacttaagt cgntagcgtt      600
ccttataaac cncctacagg cagaccccct tgtaaacggc tcgggggt      647
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<210> 635  
 <211> 645  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(645)  
 <223> n = A,T,C or G

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<400> 635
ccttcggctt ggggtttttt ctgagcccc ccccccccc ccgaaactc gccttaccct      60
agatacccaa agaatagttc cactcaactt cgtctaagta aaactctaga acttccaaac      120
ataaaagact tcgcgcggtt agctacacag cctacgggaa tctcacgaat ccgattcaa      180
gtcccactct cgaccacacc ccggtatcgt cgttttccca taccaatgtc gaaaaataaa      240
ataaaatcca gtcaagcccc acggtaagcg ggggtagggc taggcgaaga ggcaggaacc      300
gttcgaggcc gggggctttc aaaatacaaa acaactactt aaagtttacc cttctaaag      360
tcgggggcaa cgggttaaagc acgcctctaa agtactactc gtttcgagaa ggggtagtca      420
tctcccgcat agagactctc gcgtatatca actcgcacgc cttctagcat tccgacggtc      480
gccgcggctt acatatcttg cggattagct ccgagggact ataggggtta ttagtctagt      540
aaattctctt agaggatagt cggggtcgta gttaggcagt acgaggggac atggnctgct      600
tcgtgctcta ccttgacagc atactcttat aaacatcttt ttccct      645
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<210> 636  
 <211> 643  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(643)  
 <223> n = A,T,C or G

<400> 636

226

ccttcgggctt	gggttttttt	ctgaccccc	ccccccccc	cctagcggaa	aacaatcccc	60
accgagattt	tattaatcgt	aaaactcgcc	ttcggtagca	agtcttctc	cttcccgtaa	120
cctggctccc	tcctagnngc	tttacgaacg	tcctctctct	tcttacggct	cggagagtgt	180
tacggttaaa	tccggaggng	gggctaacga	atccaaggct	aactcctctt	anagtttggt	240
gtccncncgt	ttagtaagga	tccgtggagg	gcgagtattt	gnccccggc	ctttattnta	300
tagttcccta	gtacgataaa	gntaccggct	atcctattac	agcggataaa	agttatttan	360
agggccgacg	tcnccgctag	acaggctaca	gctagnngag	gtaccgcctc	cgactantcc	420
gttgnntccg	acaaggngt	tccggttaac	tccacaaact	cctccgcgca	ctctanggtg	480
gggacggcag	ttccncngtt	tagtgtgcgt	tatagagaag	ggcatttgag	ttggacgtta	540
cnthtttaaca	taggttattc	cgtttaggtt	cttgccgggc	cgtgggggta	gtncnccggc	600
gcgttnttat	cggcgatttt	cgcaggtttc	cgtttccggg	tnt		643

&lt;210&gt; 637

&lt;211&gt; 631

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(631)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 637

gggttntctc	atttgggtgg	actttttggg	tcgtaggaac	cggtatgnag	gagtaggagt	60
cgctgggaag	actagaagtt	agctacggac	gattagtgtg	attccactct	taataacgag	120
taatcgttta	cgtcgggttg	gtgtttcggg	gttttgaga	gtaagcgtag	ttgtggagtt	180
tcgcatatag	gtccccttac	ttcggcgatc	tcgtcttctg	tcggttagg	tattattggt	240
catccttcgc	attagtagta	gggttggtcg	gataaatcga	tagctattct	ttagaattcg	300
tagtcggaga	attcgtgtac	gaagtccttt	aagttcttta	agttcgcgag	taagacgtgt	360
acggttattt	tgctgctgac	gtagggtgtc	tttacgggag	tttcgtttta	ggggtttacg	420
tagaacgtta	ttaagcacgg	taatacgata	gaggattacg	cgacgtattc	gtcttagaac	480
gtcgattttt	cgaaggcgca	tttgttatcg	aaggggagtc	cttgagagaat	cgagatatct	540
caagaatatt	acggagatta	cagatcggaa	ggctcccag	atcggacgta	ttaccggtct	600
cgcccgaaac	gagtaggtat	cntccggata	a			631

&lt;210&gt; 638

&lt;211&gt; 606

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(606)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 638

ccccccccc	ctcaaccatc	nattccccac	ctcaacgcga	attacggttt	cgaaagtcga	60
caataagtc	ggtcgagtag	agggaaatcag	gggctgggtan	aaaggaccac	gggcggaaaa	120
taccggtctc	cttccgggga	gcgacgtcgg	ggaaagggaa	gagagcggtc	tagttcgtag	180
gcaaacagg	cagaaaaagt	aagggttaag	gtcggagggg	agaggatagc	tagtacgctt	240
agttcggggc	tcgggcccag	ggccactttc	ctctttcgcg	ttcctttact	ctgcttacga	300
gttcaggctc	cggagttccg	cgccggagg	cgctgcgacg	ctaggaatgg	ggactcgctc	360
agtccecggt	tatccttcgg	gattctatgt	tttcgccgat	agacggagac	cgggtagtag	420
ggttccgctg	taccgccact	cgctgccttg	atccggcccc	ctccgcttaa	gggcgatgaa	480
agattaggt	ttagggctct	acgggacgag	gcataggg	ggagaagggg	ggaggggtcg	540
ggggtcgaag	ggantaagaa	atcgcantcg	cgcggggctg	gtagganccg	aaatttttct	600
cnncgt						606

227

<210> 639  
 <211> 592  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(592)  
 <223> n = A,T,C or G

<400> 639  
 tccntcggct tgggtttttt tctgagcccc cccccccccc cccccgggaa cgagaaaaca 60  
 atcccaccct accgcgggga gtgggttgna cgcttagttc tagaatcctc ggaatcgtcc 120  
 tccggcgttg gtagttccgg cgattccgag tatgccgaag tgtatcgctc cgtctagagg 180  
 ttggtatctg tttatcgcg aacgctatt gactcggatg ctttcgaagt agggggatag 240  
 gcgcatagat acgcctccgc ggtgtcctct gaagtggccg catccgtgga cgcagcgtag 300  
 acagctctgg tggacgataa cggcttctcg tactcctact cgggctatta tgtagagag 360  
 gacttgtttc tgaacggata taccattagc gaaggggtac cctccgctaa cgcaggcgtt 420  
 tctaacagtt cttccgggcy ctcgaattt agattgacgc ctccgcagca ttgtgggata 480  
 ctcttcggtt agccctcttt ataggatttc tcctccgcc cgaaganggg ctggtcgtcc 540  
 ccggcangta tgtctagctc gaacgctttg ttactccttt gttttcgaaa na 592

<210> 640  
 <211> 637  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(637)  
 <223> n = A,T,C or G

<400> 640  
 ctttgtggcg gtggntgtct catttgggtg gacttttttg gtcgtaggct tatccgggtn 60  
 gggctcccga agtagcttag gatcgccggc tagttccggt cccgcccgtc gaaagcgcgg 120  
 ttccggcggc ggccccgct togttcgcgg gctttaccct catagagtgc caggtctcgg 180  
 ttcttacggg ttcgtcggcg atagatttta cggcgagagg tccgtatctt cgcgcgttta 240  
 cgttcgggtcg gcatctacgc ctagtccaca ggtagtttat ggcgccggagc gcgtgacgga 300  
 gaggttatatc gggacgcgga agaaccgcct ccaaagtact agtacaggct cgttcgggcy 360  
 tagatctcct cgtcgggtcg gcggttctta cttctagggc cgtctacagg tttaaggcgg 420  
 tcgttagatc tttagaaacta tactcaagtt tcagtccgaa gaaaggaaat agagagaagg 480  
 gtaaacgatt acctccggtt ctagcccttt ttactcgcat aacgggagaa cggggtccgg 540  
 ctctcagata cgcctcgcga gacgtcgcga ttcaacttta acctccgcta gggcatccgt 600  
 atacgggtta cgcggtaaaa gcgacctcg aaacctc 637

<210> 641  
 <211> 649  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(649)  
 <223> n = A,T,C or G

<400> 641  
 ctntgtggcg gtgggtgtct cagtttgggt ggatttttgg gtcgtaggna acctggtatg 60  
 aggtctagtt tcttcaacga ttcttggttc agttacgcga ccctatcctt atcttacaat 120

228

```

gtcttctaca tcaggttcat caattaatat atcaattaca cattaacgac ggtgtgacgc      180
aatatgagaa agtataacatt aaggttatta tatattattc gcttaaaaag gttcctgaca      240
tgggacaact tcaccaccca ttctagaagc cccccctcct gtaggacccc ctcgagttcc      300
ccattatctt agttcagttt tcatttttta accaggaggg tatcggtttt taataggtac      360
tattttgtca aacttttcag aagctttatc ttcaaatata cttgcaccat ctgtactagg      420
agcactaaact attcaggtct attacagctc aacagaaaat aattgaaatt aaacaaccta      480
agtatcgctc accataaacc catcgggctc tcacccatt tcttcataag ttctagagca      540
tcctgagctc tttcctatta cccttgatgg tactcatggg ctaatacccc ccgcagttat      600
aggtccttat ggatcctatg ctaccaccgg tctaaccctt tctatcacn      649

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&lt;210&gt; 642

&lt;211&gt; 645

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(645)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 642

```

tccttcggct tgggtttttt ttctgctggg gttactatta tcgattgtta cttgtaaagg      60
cgatactccc accgctcacg atattagacc tgctcctcta gaagcgaacg gcgataggtc      120
tactcggccg gcgaagacgg cgaacgggta ggaggagcca tatgcaacc taacggagat      180
tataagtact gggaaaaata ctagtattaa ggtagcgggt taagatagggt ggagagacac      240
tattcacgag cataagcact tagaagggtc tctcgaggag aggtaggcta cggactacgt      300
tccttcttcc tctagcctcg agaggagta tagatgatte gcaaaagaga atccctccta      360
tacgctggca taactagacg acgcgtcgtc gggaaatctc gccaaacccta ttgcgacctc      420
caaaaggaag attgtcgttt catagaacgc taataactccg ggtcttcccg aatcatagcc      480
gcatatcggt aagaagacgg taaaatcgcg cgattctaac aagattctgt agacttaagg      540
ctaagcacta gaagcgatct cgattccgga tcttaagatc atactaatag ttcggtcaca      600
ccagacgacg attagccact agaagcccta ctccgtngaa accgg      645

```

&lt;210&gt; 643

&lt;211&gt; 586

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(586)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 643

```

ctttgtggcg gcggtgtctc atttgggtgg atttttgggt cgtaggaacc tggatgcag      60
ggtccgcccc gaattaaaag cgggatcccc aaaacgnngn ttcgcaagaa gagaagaatc      120
atagcगतag anctttcata gtacaaagggt aactaagagg aaaataatgc agattcagaa      180
ctagttgcca aattagaact cgattaggcc aaggatccga gcctggcgct atcacttcgg      240
gacttaagct acggtagagc agtcggtcct gaagcatagc tcccgtagga cgtaggaaac      300
tagtccggca cggaggacat actctcgagt ctcggaacgt ctatttagaa tataaacgca      360
ttaacctcag aaggcgccga cgcggttact ctctagggaa ctatttcatt ccttccggag      420
ctcccctatt tttccaacac atataccggc aaaggaaaat cttntgtcct cggctctaaag      480
agagggaaaa aaaacgatat ctaggttcgg gtttatocat ttaaaaanat ngacgcgact      540
actccctttc aaagggagtt tccccttagg nagagttcaa cngaag      586

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&lt;210&gt; 644

&lt;211&gt; 646

&lt;212&gt; DNA

229

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(646)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 644

ctttgtggcg	gtggttgtct	catttgggtg	gcatttttgg	gtcgtaggaa	cctggatatng	60
agggctat	gacttgtttc	tcaaatccca	tggtatggtg	ggtggcgtgc	ggggtggcgg	120
tcggttcggc	gggggtgggg	gtcgtcctcc	aaaggagttg	ctagagggct	tttagtggtt	180
ttagggcggg	aaggggttag	agcggagaga	cgtcgtcgtg	gaagcttctg	gcggagcgcg	240
agaagtagt	tagcgccggt	tcggaagatt	ctcagaattc	gagaagaggt	agtggggcgc	300
ggagagagag	tttctaagtc	taaacgtaga	ggtcgtccta	gtcgggccgg	gagtagcttt	360
taagctagag	gtcaggtcc	tcgttttaggc	tccgggctct	tcgggcagta	tcctctttct	420
cgaggaacgg	agcgaccgac	gtcgtagccg	gacccgtcta	tccttacgtt	tagagatacg	480
ctcacctcca	cgggcgtata	tgcccgata	cgtataaacg	cgtaatatatac	tcgcgcgtaa	540
aacacgtata	cactatatac	acgcctcgta	cggaccgtat	agcgttatatac	gcgcgcgtat	600
attaatttac	acttatatac	gcgttaaacac	gatatatcac	acnccg		646

&lt;210&gt; 645

&lt;211&gt; 654

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(654)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 645

nccntcggct	tgggtttttt	tctgaccccc	cccccccccc	cccccggtcg	acaacgtgcc	60
caccgttgcc	atcccagcat	agctggttcg	ttctgtttta	ttcttagtag	tttagttcgc	120
ctatagtc	tcgtctatcg	tctatcattt	aaggagcggg	ggctcgtct	ttagggcggg	180
tatcttaggt	attcttctgg	tttcggctgc	cgtctcggag	tctggtcctt	ttgctttcct	240
ttcttggtcg	aacttcgtgt	ttgatcgcgt	tgtttctttg	gggtcgtcat	acctaaagggc	300
cacttcgcca	acaaacaagt	ttgtgtagtc	gtttctatta	gggttcgctg	gccggcgctc	360
ttactggttg	gcgattttta	acgcgtttgg	ttttaatttg	cttcctcccc	tagggctcgc	420
tcggtcttct	ctctgttcgc	tgtctctcgtc	cggcctttgg	tgcggggata	gctccggcta	480
ttancgtgcc	gtgtccgtgt	ggnttttgtc	caatgtgaag	gcctaggggt	gcgggcttct	540
ttggccatgg	nttccctct	tgtgancctt	aggggtaacg	antcgttaatt	naaggtcggg	600
ggttggnata	cgttntangg	gangcctgng	tccgntattc	cttgttttgg	cctn	654

&lt;210&gt; 646

&lt;211&gt; 645

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(645)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 646

tccttcggct	tgggtttttt	tctgagcccc	cccccccccc	ccccacgcc	aagtacacag	60
accacacaaa	aacaacgtca	acacaacttc	gggtatacgg	accttaagag	agaccccgta	120
gtagacccta	ccacagccat	ccaatagtca	aacaacaagg	gcgcacccaa	tccatccata	180
gagctatcaa	acaacggagg	ggaaaggaaa	gagcagggtc	aacttagcag	agatcgaagt	240

230

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cggcactaat tcctttcaag tactcgctcg gctttagtgg cggggtaaag tccgctctca 300
aagggccaac gaggttttaa agcgaccccc gtatcgagtc ttcttctgtat tcattaaggc 360
gttaaaggta cgagacctag aagagagtag aattagccca ccaaatcgcc taaaccggca 420
aaaacgacca aaagtcaaag acccttacia atatacactt aaaacgcaa ccccaaaaac 480
gcgatcagta acgcaogtac ctttcccacg cttttctttc ttctactctc caaaacaaac 540
ccgaatatatt agcgcaaaaa atatacggag gagaattaga agctattacc cgaaaaaaa 600
ncgganangg antaaatngt gggaatana cgtttggttt ttctg 645

```

&lt;210&gt; 647

&lt;211&gt; 753

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(753)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 647

```

acctacctg gtacggggcc cccctcgag ttttttttt tccaaataca actcagattg 60
tatacgaaaa gctgataata cattgacttt tgctgtttta atcccttgag cctttgataa 120
tgattttttt tgtgttaaca attgtagtat ataaaatcgg attcaccatc cttctgatgc 180
catattgatt agtttgattt tatggtgatg ggatcattgt gtgttaactg tattaagaag 240
aaatggattt gattgacttt gcatccattt ttatctgtgt tactttcatg ttttatttaa 300
aagcatttct ggaccagaat aagttaagtg gtataatttg ctttttacac gtttatataa 360
ttgaagttag caatgtggca aaatctctaa tggaataaaa atgcttcaga atgatgacat 420
aaatctgagc tatttcttgc ctggagaaca agtggtattc ataataattt aatagcttct 480
gaggtgtttt gttcatgtga tgaaggctta tccacctgtg atcaattcat gggctctgct 540
ttgtttaatg tagtcagggt gtttaatacna gacttaagag tcatctactg gtgataagtg 600
gtgagtgaag attacatgtc ttangaaaat tatactggga atatctctga cattaatggg 660
tttaaattgt ttaaggctag gggatgatgc aatgganaan atncttccaa angtttctgg 720
ttgtttatat ttgnggaagn catnaagana ccg 753

```

&lt;210&gt; 648

&lt;211&gt; 383

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(383)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 648

```

gatatcccg ggaaatgcg aggcctttng gcttacgtgt ttaccgcgta gggcaaagcc 60
ttgncaaatt cccggccagc ggagcggcga ggtggtggac tcacgggaag ttaaagagcc 120
tcgtcggcgt cctcgaggct ccaaaaccag gctctaggcg gggacgactg cagccgttat 180
ggaggccacc gcggctacgg ccgcggctga ggcctcccca ggtggagcgg tggcctggag 240
gggaatcttg atcctgggac agccacctgt caagaggagg cggagcgta tgcctctgga 300
agactggatg aatattctcc aggagcctga cgaaggcgaa gaagtctttg cagaggaaat 360
tgaatgctgt ctgatgctac aat 383

```

&lt;210&gt; 649

&lt;211&gt; 349

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

231

<221> misc\_feature  
 <222> (1)...(349)  
 <223> n = A,T,C or G

<400> 649  
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 cagtgtggtg ggaattccat tgtgttggt cactagtaaa tggatttagc tagacanagg 120  
 anatttacc tttccattt agcacagtga gganaggcta nacagctagg atgcaataaa 180  
 aaaaatttta atgagaaatg tgtgtggtag attaattcta ttaatctcaa gttatagatt 240  
 aaaaaattta agtaccncat aaatgccatt tgcctttgct aangntacat ttttatgaan 300  
 aangacntg catacnaat ganatactgg actttnggna cttgangga 349

<210> 650  
 <211> 306  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(306)  
 <223> n = A,T,C or G

<400> 650  
 cattgtgttg ggagcatcct tccatcagct cccatgagaa attctctgtt gggtttaagc 60  
 aatccccaaa tatatcata tgcacatgaat atatcatctc ctcaatgtcc agcattagca 120  
 gacaagatga gtgctgaaga tgatataact cctacctctt atgtaggcta gaggtaaagt 180  
 ctggctctgc tgactgtggg gacataccga aaaggaatgt gggttaatat cagangacct 240  
 cctgcagat ccganantca gggncctggac tttctgggan aggaagcnaa aagttatntc 300  
 tgaacc 306

<210> 651  
 <211> 769  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(769)  
 <223> n = A,T,C or G

<400> 651  
 cattgtgttg ggcagggtca tttctaaggc atgggctgga agcttttatt taaaacttta 60  
 catgtcttag aagcactctg gttgttgcta ggcagacaat tttacatctc ttgctataacc 120  
 agttgcatga agttcatcat gcatattggc tgtggaaaac cttaacagca tcatgtcata 180  
 aggtttcagt aaggttttaa tgaaatcatg tattaagcac ttagtatagt gcaccttaaa 240  
 tgttagcttc aaaacaatga caacctaaact aatgttgaaa gaagcttggtg tttgtaaatt 300  
 atgtcttatt gaaagatgtc atcaaactct gttatttcta atcccttaaa gtctctcaat 360  
 gtatttcttt ttgccatatc caatgacagg accttagttt aagccagtgg ttctctcaac 420  
 ttctaattcca gagataacctg ggtgtcccca agaccttttc agagcatcct tgatgtcaaa 480  
 accattttca taataatatt aaaatattat ttgctcattg tactcttatt ctctcccaaa 540  
 tattcagcga gttttccaga agctatataa catgtggtaa catcttatca ctctgacgat 600  
 taatagaata tgnngttttg gattcttgng tttaaaattt tctcactttg gggttctaatt 660  
 atggnnacga ttaatagata tggncctccat gaccagangg ctttaaagca ntcaataatt 720  
 ttttaagagac taagnactat ccttttaaaga tngngaactc catcttaatt 769

<210> 652  
 <211> 267  
 <212> DNA



232

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(267)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 652

nnangccctt	taaccattgn	ggcctccacg	cnntggcggc	cgctctacaa	ctagnngatc	60
cgcnactcta	gnanaangat	tggctcttnt	ggngtgggcc	ggncgggctg	gggcgttaag	120
cggggctggg	cgcgcgccgn	ggttgnacna	ggcgccgccc	cccncacacn	cccggagcac	180
cctcnttgcg	gcctntcccc	gctcaccccc	cgcgcgccgn	tccgcttttt	ccncacccan	240
agcnctnttt	atctntgtct	cctccgg				267

&lt;210&gt; 653

&lt;211&gt; 501

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(501)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 653

cccnttnacc	cattgctgga	ctccacccgc	gtggcgccgc	ctctanaact	agtgggatcc	60
ttncnatgag	atgngcgang	gaggacnnat	ttgctatnct	ggatggggct	gantcntnta	120
gctnctctag	cancagatgg	gttatcgagg	aagatgactc	caangggcta	nantcctatg	180
cncatcctaa	aanncanctg	ctgtnttcag	agtaecgcgac	acatcatcnc	tnatgcattg	240
ntgancaaga	cgggcangtg	cttatccctca	gcgangatgc	ccttaaccan	gagctcgaat	300
ggacntatca	ccttanaggt	acanntnccg	caccacacac	cngcttgenn	cctgacgctg	360
gactggatcn	cttaggccac	caatnccccg	tttnccacat	ncctgggacn	ctananatac	420
tcganggggg	gcccgggtanc	caattcgccc	taatactgag	ccttgntacg	nacgctnact	480
ngngtcccta	ttanaacggt	g				501

&lt;210&gt; 654

&lt;211&gt; 710

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(710)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 654

gcgnctttan	cncatgctgg	gctccacgcg	gtggcgccgc	ctctacacta	gtggatccca	60
acactgagtc	caccacagna	aaactcanca	ccaggcagac	cccacaactg	cagaatccag	120
gctgcaattc	acagactaat	cntctagacc	cacctcagta	ccagatggta	ccacacagct	180
caaggnttta	ggtttgcgtg	gtanactcaa	tctctatctt	tcaccactgc	cagcctgact	240
tcagagatcc	tgngctctgg	acagtccctca	gtggcaggca	actctcagga	gcctcaggnt	300
tttggcacat	cccagnacca	gccagctgcc	acaggccctg	accttntanc	aacactgccc	360
atgtattcca	gacttctanc	ataccacagt	gccatgctga	ttgcatctat	agangctcag	420
gtgencctca	aanctgtgcc	tgtctcgagna	ngccccacgt	ctctggcatg	ccccaatgcc	480
atgngtggn	acanttgact	tctgggcatg	ntgggaattcc	ctaccactga	ncctgaccat	540
aggnggganc	ccattttttt	cgaggggggg	gcccggcccc	caattccncc	ntatagnag	600
ncgtanttac	gcgcnnctta	ctnggccngt	ngtttaacaa	cgctcnntgan	ctgggggaaa	660
cccctggng	cnacccaaat	taaacngcnt	tgcannacat	ccccctttcg		710

233

<210> 655  
 <211> 202  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(202)  
 <223> n = A,T,C or G

<400> 655							
cccccttttccc	ctttcancccc	ccccgtttttg	gngcgccgcn	acacctactn	catccaccca		60
cantcgacca	cccgagcttt	tttccgatcc	cancatcnat	gnggattttt	tctntgcntg		120
ctgngcctgc	acctttgnta	ggtcaagcct	ggcccatctt	cgacaacttc	ctcatcacca		180
acgatgaggc	atactctgac	ga					202

<210> 656  
 <211> 308  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(308)  
 <223> n = A,T,C or G

<400> 656							
gctgntgaaa	gaccacaccg	aaaaactctn	ctttccgact	tccacatgat	gatcngcatg		60
tggtggtgag	agacttatca	tgacgacatc	gcttccnacc	atcgcanccn	ctgcccgaagc		120
ccattcatgg	aggcctgggn	antttctgtga	ntgacntnga	cnctanacnc	tnccactgtn		180
tgctatccag	acttgnttng	aatatnttat	tggcnaaaana	canttnccgga	atgctgtgnt		240
tgnncattga	angatctgat	cactatgaga	gggtgaggac	nncctgctng	ctggcancnt		300
ntaacccn							308

<210> 657  
 <211> 696  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(696)  
 <223> n = A,T,C or G

<400> 657							
accntttcca	caatnctggn	ctccccggcg	tggcgggccgc	gtcgaccagc	aacctcagct		60
gtgggtcttg	ttacagtaat	gagttactgt	aaggaaaagt	tgacatttcg	agcaatttga		120
tttgtttaaa	aactagagca	gtttcagggg	tttcttgta	aatctgtctt	atgtgtcttc		180
aatgtttctt	cttgaggagt	agagaaagga	attgttagga	atgatgcata	aacctatggc		240
tattttatct	cgctgccacc	cataatcaga	gcagattctt	gggactatga	ccctcatgga		300
gacatgacaa	ttgtgtgtgt	ggtgggtggg	agaaaagagc	tgggaatttt	taggggtctag		360
aggtccaat	caggactatt	ttatggagct	ctgctcacca	actttaagt	agcaccagg		420
gtngaaagc	gaatcttggg	ntcaaaaana	caatggnaag	gggtaagttg	gtatnctgaa		480
ctggccactt	cggactctta	tttaactggg	tattctcant	taaggaggcn	ngggtggct		540
tggttgtna	aggaagcct	gtgcaatgga	atgacttta	aaccccccat	taaaaaaaaa		600
angntataaa	tcttgggtct	taanaangaa	gcctgggttc	tnntanocca	ttttncccc		660
gggaaggnaa	atnttcttag	gnaanggaag	ggaagg				696

234

<210> 658  
 <211> 698  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(698)  
 <223> n = A,T,C or G

<400> 658  
 ctggactccc cgcggtggcg gccgctctag aactagtggg tccgtgttgg ctcaattctc 60  
 aaggctgttg ctgtgcggcc tgttccccac acgtgctgct cagctcaggc aagcacccag 120  
 cttgtgttgt ttcatgtctc gcgtggaggc ccctcctcca ggctcgtgct ctgtgggggtt 180  
 cccatacact caggctccta ggaggagtcc atttagaaag ccagggtttt tctcagagtc 240  
 ttagttcctt gtgctgtcat ccatttcaca cgacttgggc cctgctcggg gcaacacagc 300  
 aagagaaaag acagggaaaa taagagaggg accttgcaca cacacgctct ggaccacaga 360  
 gccctgtgcc cagctcctct gtcaatacag gtggaatctc gtgcaggatc gcagggggtct 420  
 gtgatgccac caaagagcag gccgggacag ggtaggaga gaaaggagag ggaagtgggg 480  
 gtttctccta cgcactctta tttgcagagg gaaaggcggg tttgtattgg ggttgtcggg 540  
 ctttgcaccc acngcacagt tgtgagacac ccccatcctn agatcaaagc cccacataca 600  
 gcttggggaa aaacaaaacn aaacaaaaca aaaacagtaa acctccatgc canttgttgg 660  
 gnaagttttn aatttntctc ccnaccan cttgcttc 698

<210> 659  
 <211> 750  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(750)  
 <223> n = A,T,C or G

<400> 659  
 ncaantggg ctcaccgcg gtggcgccg ctctagacta gtggatcctc ctcatgggcc 60  
 tggatatctc tgaacatat atgaacattg cttatgaaaa attatttgta ngaaaattgt 120  
 gaggcctaag aatgntatct tcttttagtg atggctcttg tttgcttctg taaggnaactt 180  
 gtgggcactc gtaagcttgg atctctttta tctaatacca gntttgagat tttcttggcc 240  
 ccatagatga attaaaaact gcgtacttct tgtttacaag anggataagt ctcctagggt 300  
 aagtcttttg gggtcccaag tcaaaaagat gagggattta ccagttctct aaccttggtg 360  
 gcccagact ccaaaactttg ccttctagtc ccaagaggct atcaaaaagc aaaggccatc 420  
 ttccaccttc ttttccanaa cagcacacat tccagacagt acttgaaagc aggaacctcc 480  
 ttatccctta aaaacctctt ggaancatct tccctctctt gcttctacta tgcttggccc 540  
 acctancatt cncntttttc tggaaaccgg aaaaancttn tgacttnngt tggctacatt 600  
 cagcttggcc cctacaatn tgggtttccat ctgccctaan gaaattttta agggcacttt 660  
 tttnttggcc cctgacttct nnttttttag gctttccccc angctttgcc ccttttggtta 720  
 aaggggttat tttccttccc cttttggaag 750

<210> 660  
 <211> 849  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(849)

235

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 660

tcggatccac	tagtccagtg	tggtggaatt	cgcggccgcg	gtcgacgggc	agtagtggtg	60
tgcntntcta	aatgttataa	ttatttcaga	attactctgc	cagaaaagta	tgatcataca	120
tagaagagtt	tgtagctaac	tttgaaagta	gtggaaagtg	gttttcacgt	attgtttggg	180
ttaatttaat	tttgattata	tttggttttt	agttcaggta	atTTTTTgt	tgaaaacttc	240
aaatgacaat	ttcttcatgg	ttactaaaga	tcactcatgt	ggagtagttt	cagatttttt	300
tctgaataca	tgtattactt	ttagagatgt	aaagatgtga	aattactaag	agagaaaccc	360
atgtgatattg	tttagtggt	caaaagtcgg	tagctccttt	gacctaagt	gccactgata	420
gttaaataga	tactgaagct	atgggcaggc	tggattgata	agaaaaaagg	agacagagaa	480
atgggaaatt	tgtaaagaac	tggtcaaata	ggaaaaggag	agagcaacag	aacagaatta	540
gtaccacagt	gccgaagtgc	cacctcagg	acttccatct	cccatctcct	gaagaattca	600
gtaacagttt	gcaaatggtc	aacacaatca	tttagtgatc	ctgggttgata	ttttcaatac	660
tttctgggga	tttcttggt	ggnttcaaaa	gatgatgctg	atagttttat	tgcccctgaa	720
ggtattctga	agnttancat	aatttattgg	tcagtaaaat	atTTGaataa	aagngganga	780
aggaaaaatct	ggcntcttat	tttgggatnt	cngcnggggg	aangaggata	taattnaccc	840
cggccttgg						849

&lt;210&gt; 661

&lt;211&gt; 653

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(653)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 661

aacttaagct	tggtaccgag	ctcggatccc	tagtccagtg	tggtggaatt	cgcggccgcg	60
tcgacctcca	ttcgtttctt	gtcctttttt	ttcatttttt	ctcatgttct	attcacttta	120
ggtttctaag	ataaatatta	taaaataatt	tttacttata	aattattcac	tgataccctg	180
tctttaacat	gtgaaatgaa	ttcaaaaagga	atcctaataga	gaaataatat	actcatgatg	240
tttaatatag	ttgatttcga	aataataagc	cctctgaagt	cctaagttaa	aaataaagca	300
acttgtttga	taatttttca	tcaagaatgt	atctgagtct	ctgagtaatt	attagtagga	360
atattccatt	atcacaatta	cacagtataa	gctatttagt	ctaactttac	caaaaaaggg	420
agctacttca	acactgtgtg	agacttttaa	tgggttttga	ttgggtatgc	actattagca	480
agataaccta	ttttacagca	gtgtttntta	acctttccca	tttatttgaa	aggcagctaa	540
gatatagtag	ttaatntaan	gggctgatgc	atttatatta	catgtagana	atgggagata	600
cnaaaggagg	nggggggana	tnntttgnat	tcnnaagctt	cnttgncaat	taa	653

&lt;210&gt; 662

&lt;211&gt; 646

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(646)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 662

aaacttaagc	ttggtacccg	agctcggatc	cctagtccag	tgtggtggaa	ttcgcggccg	60
cgtcgaccca	gggacaggca	gccagnctg	gggtcaccag	ggccccctct	tgggccctcc	120
aanagcaaca	gtactggcaa	cagctgggat	ttgctgagca	cagactctgc	agcaggctcg	180
gttagctctt	ctgtgcctgt	tccttcatac	catctcaacg	cccatccatg	agatgggtcc	240
agctgttttc	agatgagaaa	atggcacagg	aagctggtaa	gtgacagtca	gaaatgaatg	300

236

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ctggcagctt antccttgga cccaccgcag tgcaggacct tgctcaacag ggatcaccct 360
tgtccgccac ctgttcacga ggccaccacg ggtttgtgtg gtcatttgtc tcctttcatc 420
tgcttgccct caaccagctg ggtcattagg gctggggaac ccagacccca cacagtcctt 480
ctcccagang ccagacacan nctncgccac agnaaggact tcagtccccg aancaaatgt 540
ncctgggcgt anaaactgna gggnccccaa tccctgggtg ggtactgctt tgcactggng 600
gaattcaccc ctcattgnna acctttccct nttnncccc ctaaac 646

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<210> 663
<211> 650
<212> DNA
<213> Homo sapien

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<220>
<221> misc_feature
<222> (1)...(650)
<223> n = A,T,C or G

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<400> 663
aacttaagct tggtagccga gctcggatcc ctagtccagt gtggtggaat tcgcggccgc 60
gtcgacgtcg acgcggcgng ccgtttcgac gcagttgata catattatta tatactacat 120
nggttttcta gaattaaaaa attaatgtgt agtgccagcc ctataggttaa gttacatata 180
tcaactctat ccaattttgt cagccataaa acttaccttt ttacataact tctaactcta 240
acaatgtgag aaatgtagat cattgcaatt ataccacaa ggcagatggc tacatgcaga 300
atggatagca gaattctagct acttacgcta gccacatggg agacgttttt tcctttgttt 360
ttgcaaaatt gcaatataag ttgcatatcg ttagagttaa aagatgtaaa gaaccatag 420
aagccagtga tgaaggacat ttatatatttc acctttacaa angaccttaa aattgcctat 480
gtggagcaga aactggagga gggcnaanc atcngtaaaa aaaattttgn tncattttgg 540
atttgggcac cattattacc tccccaggtn cctttttgnt ttaacctttc ttttaaaaaa 600
aataattcnt aatttttggg caaaaaaaaa caaggttttt attTaaattt 650

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<210> 664
<211> 678
<212> DNA
<213> Homo sapien

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<220>
<221> misc_feature
<222> (1)...(678)
<223> n = A,T,C or G

```

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<400> 664
taaaaatcta gactacacta ggaaattatt ttantatcag aagaatatca ggggtgtagt 60
actcatcana gctaaatgag agcgctttta aaatgttagt ttgtcttccg ccattttctac 120
agaaagctgc aatttcaggt tttcaacctt ataggtgata ttttaagaaa aaaaaaagca 180
atcgcaaata gccccactgc ttttacaagt cattttttct cttctaggta tagcctgtca 240
ggtggccata tgtaattttt gacatctcta ggaattttta tagaaccaga aatgggtgcc 300
agagatatgc ctgcactaat cttaagtggg gatttatgta tttctcaagc aagtgattaa 360
agcaaaaacta ggcacgattg aaatcaanat cttttaggca agaaagtcac gatgagtttt 420
anaattatct taggactctg tggctttctc ttcatagaaa tagaaaaaaa aaattgtata 480
aaaaccacaa aaggctctga atagcccaaa gcaacactga acaaaaangaa caaagcagga 540
agcaacacac taccggaatt caattatact accaaggtgt antaaccaaa acagcattct 600
attgggcata aaatagacca aagaccagt ggaacacaga taaagaancc caaaataaat 660
cctatatatta cngccccc 678

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<210> 665
<211> 694
<212> DNA
<213> Homo sapien

```

237

<220>  
 <221> misc\_feature  
 <222> (1)...(694)  
 <223> n = A,T,C or G

<400> 665  
 cttttcaaatt cttttttnct cttctaggta tancctgtca ggtggcctaa tgtaattttt 60  
 gacatctcta ngaattttta tagaaccaga aatgggtgcc agagatatgc ctgcactaat 120  
 cttaagtggg gatttatgta ttctcaagc aagtgattaa agcaaaacta ggcacgattg 180  
 aaatcaagat cttttaggca anaaagtcac gatgagtttt agaattattt taggactctg 240  
 tggctttctc ttcatagaaa tagaaaaaaa aattgtataa aaccacaaaa ggtcctgaat 300  
 agccaaagca aactganca aaaagaacan agcagggaag caacacacta ccngaattca 360  
 aattatacta ccagggtgta gtaacaaaaa cagcattcta ttggcataaa atagacacca 420  
 agaccaatgg ancagaataa agaaccacac aaataaatcc atatatntac cgccanctga 480  
 ttatcaataa cnaacaccaa gaacatatnt taagggaent nctattcaat aantagtgt 540  
 ggnaaaaact gggaaatcca tatgcagaaa naatgaaact agaccctat ccctcaccat 600  
 acgcaaannt caacttcgga atgggattac aaaacttaag acattccaac ccaagaaact 660  
 atnaaancta ctattaagaa aacagatcnc nccc 694

<210> 666  
 <211> 705  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(705)  
 <223> n = A,T,C or G

<400> 666  
 tttaaaaaatt tagatacact angaaaatta ttttagtatac agaagaatat caggggggtgt 60  
 agtactcatc agagctaaat gagagcgctt taaaaatgtt agtttgtctt ccgccatttc 120  
 tacagaaagc tgcaatttca ggttttcaac ctaatagggtg atatttaaga aaaaaaaaaa 180  
 gcaatcgcaa atagcccccac tgcttttaca aatcattttt tctcttctag gtatagcctg 240  
 tcaggtggcc taatgtaatt ttgacatct ctaggaattt taatagaacc agaaatgggt 300  
 gccagagata tgcctgcaat aatcttaagt ggggatttat gtatttctca agcaagtgt 360  
 taaagcaaaa ctaggcacga ttgaaatcaa gatcttttag gcaagaaagt catgatgagt 420  
 tttanaatta ttttaggact ctgtggcttt ctcttcataa aaatagaaaa aaaaattgta 480  
 taaaaccaca aaaggtcctg aatagcccaa gcaacactga acaaaaagaa caaagcagga 540  
 agcaacacac taccgaattt caaattatc taccaggtg tagtaaccac aacagcattc 600  
 tattgggcnt aaaatagacc naagaccaat ggaacagaat aaagaaccca aaataaatcc 660  
 atatttttac agccagctna ttatcaataa aaacnccaag aacnt 705

<210> 667  
 <211> 817  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(817)  
 <223> n = A,T,C or G

<400> 667  
 nnangacttt tgtggtntta tacaattntt ttttctattt ctatgaagag aaagccacag 60  
 agtcctaaaa taattctaaa actcatcatg actttcttgc ctaaaagatc ttgatttcaa 120  
 tcgtgcctag ttttgcttta atcacttgcg tgagaaatac ataatcccc acttaagatt 180

238

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agtgcaggca tatctctggc acccatttct ggttctatta aaattcctag agatgtcaaa 240
aattacatta ggccacctga caggctatac ctagaagaga aaaaatgatt tgtaaaagca 300
gtggggctat ttgcgattgc tttttttttt tcttaaatac cacctattag gttgaaaacc 360
tgaaattgca gctttctgta gaaatggcgg aagacaaact aacattttta aagcgtcttc 420
atttagctct gatgagtact acaccctga tattcttctg atactaaaat aattttccta 480
gtgtagtcta aactttttta aaaagacatg taatccgagg agtttgtaac tcaaaacgag 540
tgcacttagg aggtatcgca agccgtttct ggattaaatt cccagctagc ttgcttgctt 600
agcaggggag ggnaaanaag acatctgcag cctagggaag aaaacctttc gcattgttct 660
tacgtgttta cgttattttta ttctctanaa caaggcngaa ttgggactcg aatgggttcag 720
ttgggggtggg ggatcccctg gtncataaaa ngtcanaaag anggtacagg cggaacncca 780
agggtcgtcc tgcatttana ctcggaattt tgggtgcc 817

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&lt;210&gt; 668

&lt;211&gt; 826

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(826)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 668

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cgggggggnt tacgtctctc tggacgcttt tattgtacca gggcgatccc agcccaactg 60
taccattcga gtccctactc ctgccttgct ctagggaaat aaaataacgt aaacacgtaa 120
gaacaatgag aaagcggtttt ctccoctagg ctgcagattg tcttcttcac cgccccctgt 180
tagctagcta gctagctggg aatttaatcc agaaacggct tgcgatacct cctagatgca 240
ctcggtttga gttacaaact ccgcggatta catgtctttt taaaaaagtt tagactacac 300
tagggaaaat tattttagta tcagaagaat atcagggggt gtagtactca tcagagctna 360
atgagagcgc tttaaaaatg ttagtttgct ttccgccatt tctacagaaa gctgcaattt 420
cagggtttca ncctaatagg tgatatntaa gaaaaaaaaa acaatcgcan atagcccact 480
gcttttacaa atcattttttc tcttctaggt atagcctgtc aggtggccta atgtattttt 540
gacactctta ggaattttta tagaccagaa atgggtgccg gagatatgcc tgcactaatc 600
ttaagtgggg atttatgtat ttctcaanca agtgatttaa gcaaaactag gcacgaatga 660
aatcaagatc tttaggccag aaatcatgaa nanttttana attattttan gaatctgtgg 720
cttctcttct taaaatngaa aaaaaaattg tttaaaccca naaggctctga ataccaagc 780
nccctgaacn anagaacaan gccggagcac cccctcccaa atcccc 826

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&lt;210&gt; 669

&lt;211&gt; 547

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(547)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 669

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cattgtgttg gggaaaaaat gatttgtata agcagtgggg ctatttgcca ttgctttttt 60
tttttcttaa atatcaccta ttaggttgaa aacctgaaat tgcagctttc tgtagaaatg 120
gcggaagaca aactaacatt tttaaagcgc tctcatttag ctctgatgag tactacaccc 180
ctnatattct tctgatacta aaataatttt cctagtgtag tctaaacttt tttaaaaaga 240
catgtaatcc gcggagtttag taactcaaaa cgagtgcac tnggaagtat cgcagccgtt 300
nctggatnaa attcccagct tgctngcttg cttagccggg gggcggtnaa aaaaacatct 360
gcagcccnng ggnaaaaacc ttgcattgt ttacgttatt ttatttcctt 420
nnagcaaggc nggganttgg ggactcgaaa tggtagagtt gggctgggga tcgcccttgt 480
tacataaaag ncgtccagaa gagggacggt tacaggcnng ganctccaaa ggtcagtcct 540

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tgccatt 547

<210> 670  
 <211> 232  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(232)  
 <223> n = A,T,C or G

<400> 670  
 cgaactatatt agactaccta ggaaaattat ttagtatca gaagaatata aggggtgtag 60  
 tactcatcag agctaaatga gagcgcttta aaaatgtag tttgtttcc gccatttcta 120  
 cagaaagctg caatttcagg ttttcaacct aataggtgat atttaanaaa aaaaaaagc 180  
 aatcgcaaat agccccactg cttttacaaa tcattttttc cccaacacaa tg 232

<210> 671  
 <211> 214  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(214)  
 <223> n = A,T,C or G

<400> 671  
 ctcccccttc ntccttcgct actnncatt ttcnnaaatt tntttcgcnt atgnnggaaaa 60  
 acaccacat tnttcanctc gcacagaaca ngnnnggggtg tgtaaaatga agggcttccn 120  
 cncctttctct tattnaanaa cactnaaana ggganggggt aaaacccgcg ngatntctac 180  
 nctatcgcg gcgcttttgg ngttggctag aaga 214

<210> 672  
 <211> 328  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(328)  
 <223> n = A,T,C or G

<400> 672  
 ngancagcgg ngtttaaacg ggccctctaga ctcgaggaga cncctgttgg atggtggatc 60  
 acanntcgnt actactatac aggacagagt atcggganct cttggntgtt ggngcctgcc 120  
 aaccactgct nctgttaact gcgtatctga agggactcgg actggcttca gaagaactac 180  
 cggtcgaat gnaccatgga tgattcncnc tagttgaaaa aaaactcagg cacatgtatt 240  
 gccactgatg actagcgcca gactnctctc ggctctntaa cgagcccaca tgnctgtgtg 300  
 ncncctgtgc tgnctccaga agaggttc 328

<210> 673  
 <211> 223  
 <212> DNA  
 <213> Homo sapien

<220>



240

<221> misc\_feature  
 <222> (1)...(223)  
 <223> n = A,T,C or G

<400> 673  
 gggggc aaag ctggctagcg tttaaactta agcttggtac cgagctcgga tcccnagac 60  
 attgtgcatg aaaatgcaaa ttgagtgtgg tctatantgc catcntcacc tntgncngc 120  
 tcaaaacaac ngctttctgc tgcaatgggt agggctcctn acncacggtc gcnnacggag 180  
 gccncttat cctcntcggg nnggatccct ngaagcatnt tct 223

<210> 674  
 <211> 256  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(256)  
 <223> n = A,T,C or G

<400> 674  
 gnggggtcnt ngatgagcgc gcgtaatacn atcactntcn ggcgngntgg gtaccgggcc 60  
 cccctcnaa gcggcgccc ttttttntt tttttcatn acatgataa ntcttnttc 120  
 taaacagacc acaccactan agttccttn cttngtacg gaattgagtt aaagtagagn 180  
 atacaatgca gggcttcnnc tctatttcac attccaggnt ggttcngnat ggatcgcccc 240  
 tgcctctcgc atgggt 256

<210> 675  
 <211> 439  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(439)  
 <223> n = A,T,C or G

<400> 675  
 nnactagtcc agtgtggtgg aattccattg tgttgggctt gtatgggttt tttgtctag 60  
 ttntttggga aatgttngtg ttactatntt ttggatatna tatatgatat gtatggccct 120  
 tctatgggct cctcanacng aactcaacca ttttccacaa aaccnattcc tcctttccct 180  
 tcatgactga gtgggtgttg tactatccng gaaactggga cattgtcctt cacatctntc 240  
 ccttanctgc ctngtccnat tgatgtcttt gagctntgan atgtctttgt taactntctc 300  
 ctncntctgt actgccggca naattaagca ccatntgtca caaaaagtat tgcgttacct 360  
 tcacgnatct gttngttnc atncttgctg cttctcngn ggaaaatagg ctnttctggc 420  
 aaccgaacng aanaaatac 439

<210> 676  
 <211> 587  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(587)  
 <223> n = A,T,C or G

<400> 676

241

```

ngngggcctn  attaagcgcg  cgtaatacna  ctcactntgg  ggccaattgg  gtaccgggnc      60
cccctcaagt  tnatntgccn  aacctctctt  ttggaataac  aaaaggttta  acacatatgt     120
cctcataggg  acgcgccttc  acacnttcct  gacngcttca  tanacntcat  tncatatttct    180
cctcagnaca  agttnaggcn  gaaggtgagg  canacnttat  aatttccatt  tcacaaatnc     240
ggaagtgag  gctcaaagg  nttaaaaaat  aacctgatac  aantcataga  gccggtntct     300
ggaanaagca  ggagcaaagt  ccaggcatcc  tgatccaagc  tnggtccact  gccttccact     360
ctggagaggc  ttcattctcg  acaaaggaag  ggaacntgag  ggctgganaa  totcatggga     420
taaagacctc  agnatattcat  gctcctggaa  atcccatggg  ttgaacaaca  ggtntttggc     480
ccgtggttct  ntccctttgn  ccattcttta  accttggggg  aaatgatggc  ntctntnagc     540
nttttttttn  aaagagatng  aaattgaatg  attatngct  cattggg      587

```

&lt;210&gt; 677

&lt;211&gt; 444

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(444)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 677

```

gtggggcatn  attaagcgcg  cgtaatacga  ctcactatag  gggccaantg  ggtaccgggc      60
ccccctcgaa  ggggccgccc  tttttttttt  tttttactgt  ccaaactntc  tatngatnta     120
gttgaactgt  ncaacgattt  catgaaattc  tatacacana  gccttcaggt  ccagagagta     180
aaacaaattt  aaatttnttc  accanattgn  agcagncana  agcatccnat  natatccgac     240
tacaatgaat  natatgctna  nggtanctna  tttaccact  ntggggtctt  tanggtctgt     300
cacaaactat  tttcgtaaac  atcnntttaa  antnggtga  atggacctaa  tnccagataa     360
ntctatttna  tntacccatg  catnccgtgt  gctnactttt  cgggctgtgt  tggcntactt     420
ttaggagaaa  attggtataa  atnn      444

```

&lt;210&gt; 678

&lt;211&gt; 670

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(670)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 678

```

actagtccag  tgtggtggaa  ttccattgtg  ttgggagcag  tttaaaaaaa  aaaaagacna      60
aatatacnac  tcttgatnaa  acataaagg  acagtggctt  atgaggaana  gaaaagggtac     120
ctnaggatgc  aaaantacct  accacatgg  aaccgttngt  ccacactcat  tccnnanaaa     180
accgagtcct  ctcanttnca  cacgtgtacg  tttcagttgg  gaagtgcttg  ccattactcc     240
naagcctaga  accttcacgt  cctgaagg  ctggaagg  tttcagattg  cttaaganac     300
gnggcccttc  catattntc  tccactacc  nggggaacgg  aacaaatgga  gctgcgacng     360
ggaagcgctc  cttccntcc  gaaogcttc  tttcaaacct  gctgccttc  cnggcgaatg     420
gaccggaagg  tttntctng  tcccttcanc  ccnaattact  tcctgngttg  aaaattggcc     480
tgttggtttg  caaatgcngg  aatttgttt  ctttntcat  gtccgtgtgt  gnnncnaaccg     540
gctcncctgt  tgccctccct  tngaaagg  ttcattcagg  cccgcccttt  ctctntaan     600
ngtcctaata  cggncnggac  cactcgggga  aaattttttt  ttttcgaaaa  gccgccccnt     660
ccgtccggct      670

```

&lt;210&gt; 679

&lt;211&gt; 449

&lt;212&gt; DNA

242

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(449)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 679

actagtccag	tgtggtggaa	ttccattgtg	ttgggagtag	gtctactaca	ncctacttcc	60
cctatcatan	aaganccttan	caacnttcat	gatccccccc	tcntanncct	tttcctcanc	120
tgcntcctag	tcctgtttgt	cctnttccta	acantcntaa	ganagatnac	taatnctact	180
atctctnacc	tcoggaanct	acaanacgtc	tggaactatt	cngaccccat	gcancncat	240
ntccatcgt	cctccagcc	cctncccttc	ctttacntta	ctnaacgaag	gtcgacgac	300
cctccentac	ctcccnnc	attgggnccc	aanggnactg	gacctcacga	ntacaccnac	360
tacggggnga	ctaagnctgn	aactccttac	atatntcccc	gttaccoccn	gaacncagcg	420
aacngcnaca	ccttggacnt	caagaanta				449

&lt;210&gt; 680

&lt;211&gt; 670

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(670)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 680

tttcngtggtg	gtggaattcg	cggccgcgtc	gacgagaaga	nggaggagga	naaggagaag	60
gagaagaagg	agaanaagga	ggagaaggag	aagaaggaga	agaaatcatc	atcatcatca	120
tccactgtct	ngcaactatt	taagtgttgc	antcccttga	aaacagggtac	ttttgtttca	180
atgtttggga	ccactnctga	cnatgannag	aanaccaata	aatgcttgat	naatgaaaaa	240
ncacttttt	acctgttaga	accctgaggg	taagagaant	gatgtgactc	gacttagtta	300
ccacaaacta	tgatcctagc	atnaattggg	gcctctcaac	acctcaactc	cctgtgcaag	360
aacagatttt	caatgtctac	tgatgatttt	aaatggatta	nttcctctct	ttacttctta	420
agggcatgaa	gntttatgaa	acaaaactat	ncagttccag	acgcttaacc	cacatagtgt	480
taatagtcac	cttcaacaca	cnactaaacc	cccaaaaaan	gntttttacg	gngtttcgac	540
agttttcttt	tctttttgac	ttgnttaaca	cccnngacaa	ctttgtncetn	tttccttgaa	600
tcacancttt	cnaanancca	atggtncggg	ttttctctnt	tcngggccct	tccttnttn	660
aaaaccanac						670

&lt;210&gt; 681

&lt;211&gt; 494

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(494)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 681

tcatggtgtc	cacagtctga	tgtgagcgca	ttaaatttaa	ggatctccgc	ccttctcctt	60
aaaactcagg	acttggcaat	gancctagga	agcgcccctc	ccctcccan	ccanaccaa	120
gccccggacc	gctgcgnctc	cagctgcgcc	tagtgaaacc	gccgaattcg	aattcacact	180
cggnngggccg	gcgaagggtg	gcgcgccgc	gggagcgccg	ggcnagccc	gagggactgc	240
aagccaanaa	nggaggcatg	ggtggcgggg	ggcgccgtct	gatccaggaa	ggagcggagg	300
cgccgatcac	acactcttna	gacgccttgc	ccgcgccttg	ccagcgcgca	gnctgcagga	360

243

cgcgcgaggc aggaactcgc tggagtttgc caagccccan gnetctggaa agtntgtagc 420  
 tccctttcgg ancgnctcct ctggcccttt gggacgggtg tgtcattggg cgggggtctg 480  
 tataaggggg ggac 494

<210> 682  
 <211> 263  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(263)  
 <223> n = A,T,C or G

<400> 682  
 tgatcattca agcgntgngc gnataacgat tgctnagccc aacctttcat agggctcgttc 60  
 ctttggaat nggatgtcta ttgaatggca gggatagggg cactcggcat tcgcctctgg 120  
 tacagttttg catatataat ctcacgcga gcgagcgtag gggancgtta agtttgggga 180  
 aatgccnccg catgnccctn ccggagctta aacccccaac aatnccatt ttnaaaaaag 240  
 nttnttant taaaaaaaaa aac 263

<210> 683  
 <211> 255  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(255)  
 <223> n = A,T,C or G

<400> 683  
 cttgccggc atgcacagac ntntttacgg acacnctact ccaagngagc ctgnanctgt 60  
 ctacgggtcaa nctctaagg tngncantgc cacanatggc atagtccga gggcggtan 120  
 tctggantgc tctctgcact tgaacntaaa gcgntttca aganaggnet aatngcctgc 180  
 ctcttgacaa cnaacaancc cacaccnacc tangaccctn tangcaagga ctggattctg 240  
 naaatgcaat acaca 255

<210> 684  
 <211> 922  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(922)  
 <223> n = A,T,C or G

<400> 684  
 acccttcatt tcatgtgott ctattttcct acatctttta catgactaag ggattaatga 60  
 aatcacctot tcataatcat gaccataatt tcatacaaca agtactcaag tttgggtgta 120  
 gcactttatt aatgcttaag aattctctct ctctccctct ttctcttttc cttagtcctt 180  
 gcacaataag gatttttgaa tgtataatat catcttaggt aagctttcat atggtttttg 240  
 catatgaagc ttagtactgt cataagccat accaagcctg tggagtatgg catgattttc 300  
 attacataat ccaatgaaaa tagacttatt ttaaatccct aactttgtag ttttaatttg 360  
 tatttcacta tcttgaaatt aacagctagt acttatccat cacagcagtc tcctactgac 420  
 atgaagcaag ttgttgaatg cagtaganca tgaatgaaag catttaatgt tanacaaaaa 480  
 tgggtgatac ccaagcattc tgaattattt gcatcaagga atgggacatg tacattagt 540

244

```

gcatcatttc taccaatatg tgacttgaat tgttttttta aaaaaaggan aatgantttc 600
tcaatttgct ttaaaaaatt ttnaaaaagt tcaatggcat gctgctttgt ctggacttaa 660
tttattaaca attnttaanc cttccttaag gacanaattt tgggtgttcag gatcnccttg 720
aagggtctta tttttntan nattccaaac ccaaaaagggtg gtttaaaatg ggnggggttc 780
cccncaaaa atttgaccg gcttttttat atttaaaaaa ntnccnttt gngtttgaaa 840
nctnaatacc aattaagggg gaattttacc tnccagtggg aaaaaaaac nctngccntt 900
naaaaaattc ccnggagnca at 922

```

&lt;210&gt; 685

&lt;211&gt; 531

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(531)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 685

```

tgaggctctg taaaactggt cctctgctag gcatacttca tattctctat attaaactca 60
tctttaattg gcattggaaga ttcatgttc caaatctcag atgaagatcc tatattggat 120
gcaattaagc ctggcagcgc cctcaaaaga cagtcttgct actgctagcc acagccagga 180
cacagtaaca gtctcttcta gtgaccnag accataanaa atananatct aaagaattct 240
gactccaaag gcattagccc attcctggta ttgccaatga tgatagaaaa aattgccaaag 300
ctcctgggac atggaaatac actcagtaca tttgagaact ggagaactan tttccaaaat 360
agtatgaaga catganggtg attgtagata tntgagtttg gagaanttga gggaaatcng 420
attacacatg tttactacaa gagatgttna taagtaaaga aggcctgata tacaatctaa 480
cagacnantg agataaatct taantcacia ctgaentccc ttttggggcg g 531

```

&lt;210&gt; 686

&lt;211&gt; 336

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(336)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 686

```

ggngncctna tgagcgcgcg taatacgatc atatagggcg aattgggtac cgggcccccc 60
tcaagaacac tacaagctat gtctcttct canagagccc tgaantttta acatattgaa 120
agctctnatc ttgccaaana actccactta acttcaaaac acaccctcca cacacatcat 180
gatcaactna gatcttactg aaccagaatc ctnaatggca tacttcagga acaggggtcc 240
anagaagcag ttctcaaant gcagctnaaa aagaaactga aaaccaat catgcaanac 300
ctagggttta tttgagagca tttccagt cagatt 336

```

&lt;210&gt; 687

&lt;211&gt; 271

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(271)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 687

245

```

aatctgcact ggaaaatgct ctaaaaataag ccctaggtct tgcatgaatt ggggttttcag    60
tttcttttta agctgcactt tgagaactgc ttctctggac ccctgttcct gaagtatgcc    120
athtagatt ctggttcagt aagatctcag ttaatcatga tgtgtgtgga ggggtgtgtt    180
tgaagttnag tggagttctt tggcaagatc agagctttca atatgttnaa acttcagggc    240
tctctgagaa gaggacatag cttgtagtgt t          271

```

<210> 688  
 <211> 740  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(740)  
 <223> n = A,T,C or G

```

<400> 688
tgatgaagcg cgcgtnttac nactcactat nggggcgaan tatgggtacc gggnccccct    60
cgaagcggcc gccctttttt tntttttttg tgagagtta aataaaatat ttgagtttaa    120
tttaaagttt gagtttaatt aaaatatatg gcatatccca agttgggctt tgcanaaaga    180
acacttctca ggaactgtta gttgggtgac caggaactca gaagggtcct gttattaaat    240
atatttgga aatgcatgga ttctctgaan atcnctctgc atgtgagcaa cacttacatc    300
ncaaaccaaa attggcattg catacatnaa ccaatatttc ccaaacattt ctggttatgg    360
cccacccctt ttgtgtanta cttattgctg ttttttgga ccctggggaa attacttaaa    420
atattcagct ggaaattaca ggcgttactt ttaaggganc aagaattaca gtgactccca    480
aaattgcaag tgttgattac tatttaagaa cccaagaatt tgaaagaaat tttgaaaagt    540
gaaaacngga aatnttaaat gacttctcaa attttgaaaa ctcnngnaaa catctccact    600
ttggtncctt tccttttaaaa attggctaaa aattntttnt tatnccacc ccattggaan    660
tncccccccc ctggaacaat tggattcccc tatttcttaa aaaacggccn cccccccggg    720
ggngaacncc nacnttttgn          740

```

<210> 689  
 <211> 635  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(635)  
 <223> n = A,T,C or G

```

<400> 689
actagtccag tgtgggtgga ttccattgtg ttgggattac atatactttt agcaattttt    60
aaagaagtgt acaaagttga gatgtttcct gagctctcat atatctgana atgtcatttt    120
acatctccgt cttcacctct caaaacttct ttcaattctt tggctcttaa tagtaatcaa    180
cacttgcact ctggagtcac tgtaattctt gctcctttac agctacnctt gttatttcca    240
gctgaatatt tttagttatt tcccagggtt ccaaaaaaca gcaataagta ctacacaaag    300
gggggtggcc ataaccagaa atgtttggga aatactggct catgtatgca atgccaaatc    360
tggtttgcna ttgtantgtt gctcacatgc agagtgaatc ttcaaanaat ccatgcattt    420
tccaaatata ttttaataca gggaaccttc tganttctg gntacaccaa ctaacagttc    480
ctgaaaaatg ttctttctgc aaaacccaac ttggggatat gccatatatt ttaattaaac    540
tcaaacttta aattaaactn caattatttt attttaaaact cctcaaaaaa aaaaaaaaaa    600
agggggggcc cttccaangg ggggnccggt tcccc          635

```

<210> 690  
 <211> 3923  
 <212> DNA  
 <213> Homo sapien

&lt;400&gt; 690

acagaagaaa	tagcaagtgc	cgagaagctg	gcatcagaaa	aacagagggg	agattttgtgt	60
ggctgcagcc	gagggagacc	aggaagatct	gcatggtggg	aaggacctga	tgatacagag	120
gaattacaac	acataacttt	agtgtttcaa	tgaacaccaa	gataaataag	tgaagagcta	180
gtccgctgtg	agtctcctca	gtgacacagc	gtcggatcac	catcgacggc	actttctgag	240
tactcagtgc	agcaaagaaa	gactacagac	atctcaatgg	caggggtgag	aaataagaaa	300
ggctgctgac	tttaccatct	gagggcacac	atctgctgaa	atggagataa	ttaacatcac	360
tagaaacagc	aagatgacaa	tataatgtct	aagtagtgac	atgtttttgc	acattttocag	420
cccctttaaa	tatccacaca	cacaggaagc	acaaaaggaa	gcacagagat	ccctggggaga	480
aatgcccggc	cgccatcttg	ggtcatcgat	gagcctcgcc	ctgtgcctgg	tcccgtttgt	540
gagggaaagg	cattagaaaa	tgaattgatg	tgttccttaa	aggatgggca	ggaaaacaga	600
tctgtgtgtg	gatattttatt	tgaacgggat	tacagatttg	aaatgaagtc	acaaagtgag	660
cattaccaat	gagaggaaaa	cagacgagaa	aatcttgatg	gcttcacaag	acatgcaaca	720
aacaaaatgg	aatactgtga	tgacatgagg	cagccaagct	ggggaggaga	taaccacggg	780
gcagaggggc	aggattctgg	ccctgctgcc	taaactgtgc	gttcataacc	aaatcatttc	840
atattttctaa	ccctcaaaac	aaagctgttg	taatatctga	tctctacggt	tccttctggg	900
cccaacattc	tccatatatc	cagccacact	catttttaat	atttagttcc	cagatctgta	960
ctgtgacctt	tctacactgt	agaataacct	tactcatttt	gttcaaagac	ccttcgtgtt	1020
gctgcctaatt	atgtagctga	ctgtttttcc	taaggagttg	tctggcccag	gggatctgtg	1080
aacaggctgg	gaagcatctc	aagatctttc	caggggtata	cttactagca	cacagcatga	1140
tcattacgga	gtgaattatc	taatcaacat	catcctcagt	gtctttgccc	atactgaaat	1200
tcattttccca	cttttgtgcc	cattctcaag	acctcaaaat	gtcattccat	taatacaca	1260
ggattaactt	tttttttttaa	cctggaagaa	ttcaatgtta	catgcagcta	tgggaattta	1320
attacatatt	ttgtttttcca	gtgcaaagat	gactaagtcc	tttatccctc	ccctttgttt	1380
agctttttttt	ccagtataaa	gttaaaatgc	ttagcctttg	actgaggctg	tatacagcac	1440
agcctctccc	catccctcca	gccttatctg	tcatcaccat	caaccctcc	cataccacct	1500
aaacaaaatc	taacttgtaa	ttccttgaac	atgtcaggac	atacattatt	ccttctgcct	1560
gagaagctct	tccttgtctc	ttaaatctag	aatgatgtaa	agttttgaat	aagttgacta	1620
tcttacttca	tgcaaagaag	ggacacatat	gagattcatc	atcacatgag	acagcaaata	1680
ctaaaagtgt	aatttgatta	taagagttta	gataaatata	tgaatgcaa	gagccacaga	1740
gggaatgttt	atggggcacg	tttgtaagcc	tgggatgtga	agcaaaggca	gggaacctca	1800
tagtatctta	tataatatc	ttcattttct	tatctctatc	acaatatcca	acaagctttt	1860
cacagaattc	atgcagtga	aatccccaac	ggttaacctt	atccatttca	tgggtgagtc	1920
gctttagaat	tttggcaaat	catactggtc	acttatctca	actttgagat	gtgtttgtcc	1980
ttgtagttaa	ttgaaagaaa	tagggcactc	ttgtgagcca	ctttaggggt	cactcctggc	2040
aataaagaat	ttacaaagag	ctactcagga	ccagttgtta	agagctctgt	gtgtgtgtgt	2100
gtgtgtgtgt	gagtgtacat	gccaaagtgt	gcctctctct	cttgacccat	tatttcagac	2160
ttaaaacaag	catgttttca	aatggcacta	tgagctgcc	atgatgtatc	accaccatat	2220
ctcattatct	tccagtaaat	gtgataataa	tgatcatctg	taacataaaa	aaagtttgac	2280
ttcacaaaag	cagctggaaa	tggaacaacca	caatatgcac	aaatctaact	cctaccatca	2340
gctacacact	gcttgacata	tattgttaga	agcacctcgc	atttgtgggt	tctcttaagc	2400
aaaataacttg	catttaggtct	cagctggggc	tgtgcatcag	gcggtttgag	aaatattcaa	2460
ttctcagcag	aagccagaat	ttgaattccc	tcatctttta	ggaatcattt	accaggtttg	2520
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247

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<210> 691  
 <211> 882  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(882)  
 <223> n = A,T,C or G

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<400> 691
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aaaataaaac tagtataagg atagaagccc aggggttgatt taagtctgcg gaaatcataa 180
accataggtc agacttctca ttgatgaggt acttggtggg tagaatacaa ttaggtatat 240
ttggtctaga aaccaggatg gaattagaga ataaaagact gagcaatagc atgtttagt 300
attagaaata ctatagaaat aggaaaagcc ctgattatga ctttggagtt ctgatccaac 360
atctgggatt atttagatat tttaaaggaa aacgatgact tttagctctc aggatgttag 420
tttctcaaac cataaaatga agagcctcga aaagatttgc tttaccagat ttttctgaa 480
gtcaattcca gttctaaaaa tccatcactg ngcactaagg caaattgaat tgaataaagt 540
attgggnatg cataaaatac tctattttta aaaangaata gtaattatcc attggnaaac 600
gacgcantca tccagnatc tctaccctg nccatgncn tatgtagana tgtantctca 660
atcccttaac aaaccgattt tgcaaaaggag cttanccttg gggtaacttg tcanggcaac 720
tggtctactt tnaagactca tcttcaacta ctgggcacca aatncctacc attgcatcaa 780
actgggggtc ccatncaagg caaaccctgn gaaatcttta atcccgaat tggcgcccac 840
tttngngggg tttccnaaaa gaatcntccc ccccgagggg cc 882

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<210> 692  
 <211> 235  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(235)  
 <223> n = A,T,C or G

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<400> 692
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cttctcanag cacttaatat gttaataata aactncngga aaaaagatnt tcnatgaanc 180
nttctcttta ggaggtcagg ngagaatagt gttaatgnca ttaagganag aacga 235

```

<210> 693  
 <211> 383  
 <212> DNA  
 <213> Homo sapien



248

<220>  
<221> misc\_feature  
<222> (1)...(383)  
<223> n = A,T,C or G

<400> 693  
nttatgtaag aaatgtcata tatcttttat tttcttttaa tcaaaataaa tatgactttg 60  
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taatgcaccg catctacatt cccatgctct ctttaacttct tcagcattgc ctaaaggcat 180  
aatacacctt taattaatta attcagcctc ctaatgcaca ttaacaaagc ccctgctaga 240  
ctctgtccat aatggnaaac ctgnatgac cttgatatta acantttaag gaatgctcat 300  
ggattggtn cagacttaa aaattgaggg ggctgaanaa aatctaangg anaaatcatg 360  
gaagcatttg cacatattac ata 383

<210> 694  
<211> 204  
<212> DNA  
<213> Homo sapien

<400> 694  
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actgtccctt atttttttcc ctcccaggct cataactcga ggttaaactc tcttttatac 120  
aagaaccctg tctgatgaag catcatttca gaattttaag tcaacttaca aatgtggtat 180  
tattcacatc tgagtacaaa tttta 204

<210> 695  
<211> 670  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(670)  
<223> n = A,T,C or G

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ccagaggagg agacggaggc agagacaggc ccaccagag gaggagacgg aggagagac 300  
agggccaccc agaggaggag acggaggcag agacaggggc caccanagg aggagacgga 360  
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gagacggagg cagaanacag gccccccaa agaaganacc ggaggcanaa aacagggcca 480  
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cagggccacc caaaaggagg aagccggaag gaaaaaacag ggcccccca aaggaggaag 600  
ncggagggcn aaaaanaggg cccccccaa agngagaaaa ccnggnaggc nanaaaaccn 660  
ggggcccnnc 670

<210> 696  
<211> 317  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(317)

249

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 696

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gttagcaggg	aagagaacag	aattttatcc	accottatct	ctttagttag	tgaacaaaca	120
gcccactgtc	atcgtaggata	catttcactt	ttttocacatg	actaaggagc	tctccggagt	180
gaagagttag	taaataatgtt	tattacgcat	tcatttgcta	agaatcatca	agaacccaaa	240
gttagagacg	tttcgtgggt	gaactttctc	cctactgtct	agtagaatta	tatggggatt	300
ctggatctgc	tggtgcc					317

&lt;210&gt; 697

&lt;211&gt; 246

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(246)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 697

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tttttttct	tnacagagnt	ntttttgtgc	ccttggttct	tatgctcana	ctcngcaaaa	180
aanatcaaaa	gntacnnatg	aaaaacntat	nccatctnca	naaaggaggt	gnagntatta	240
ctttct						246

&lt;210&gt; 698

&lt;211&gt; 3674

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 698

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&lt;210&gt; 699

&lt;211&gt; 2051

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)... (2051)

&lt;223&gt; n = A, T, C or G

&lt;400&gt; 699

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251

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aaaaaaaaaa	a					2051

&lt;210&gt; 700

&lt;211&gt; 2841

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(2841)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 700

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&lt;213&gt; Homo sapien

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&lt;400&gt; 702

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&lt;213&gt; Homo sapiens

&lt;400&gt; 703

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&lt;210&gt; 704

&lt;211&gt; 4034

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 704

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&lt;210&gt; 705

&lt;211&gt; 6976

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 705

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259

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&lt;210&gt; 706

&lt;211&gt; 123

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 706

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Tyr Leu Ala Ser Val Ala Ala Phe Pro Val Ala Ala Gly Ala Thr Cys
      35              40              45
Leu Ser His Ser Val Ala Val Val Thr Ala Ser Ala Ala Leu Thr Gly
      50              55              60
Phe Thr Phe Ser Ala Leu Gln Ile Leu Pro Tyr Thr Leu Ala Ser Leu
      65              70              75              80
Tyr His Arg Glu Lys Gln Val Leu Ile Gly Gln Trp Val Glu Ser Gly
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 Lys Lys Arg Ile Pro Arg Thr Tyr Pro Ser His Leu Trp Ile Pro Gly  
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 Ala Leu Ala Pro Tyr Leu Gly Thr Gln Glu Glu Cys Leu Phe Gly Leu  
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 275 280 285  
 Arg His Tyr Asp Glu Gly Lys Ala Leu Ala Ala Ser Arg Gly Trp Cys  
 290 295 300  
 Gly Ser Arg Pro Pro Glu Thr Thr Leu Gly Ala Val Ser Gly Leu Val  
 305 310 315 320  
 Pro Leu His Pro Gly Pro Asp Phe Ser Val Arg Lys Val Gly Met Asp  
 325 330 335  
 Pro Ile Cys Ile His Gly Phe Ser Trp Val Trp Asn Ile Ser Ala Cys  
 340 345 350  
 Gly Phe Arg Lys Ala Ser Gly Cys Ser Arg Ser Leu Ile Arg Val Val  
 355 360 365  
 Ala Pro Val  
 370

<210> 709  
 <211> 141  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(141)  
 <223> n=A,T,C or G

<400> 709  
 tacggcgtgg tgcggagggc ggtacccac aaataacacn nacaccccat cctatctgtg 60  
 tccacanata aantgactca ttcctctcct cgcatanccc actntcccct ngcgataccg 120  
 taacnaance cttccccctt t 141

<210> 710  
 <211> 196  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(196)  
 <223> n=A,T,C or G

<400> 710  
 cnatccttcn cntacaccca tgangtccat gtcgcacgtc cacctcccct caaaacttgg 60  
 gtcncatcc acccgtcact ctcccntaa ncnataaccc cttttngcga atagacccca 120  
 ccttancaat nggtttttcn tttttgtcc ctnggnccgn gcgattcaan aaattgaagg 180  
 cccanaaaaa ccccct 196

262

<210> 711  
<211> 177  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(177)  
<223> n=A,T,C or G

<400> 711  
ntacntcnct ccnaatgaaa ttcgaanctc ggttaccocg gggnattocg attagngcgc 60  
tantctcgga tgtgcagtc caagtctttt gctaattctt ataattntcn ctaccctttc 120  
ttcnacaata ctgctatcct anttnttctn tcncctctct cccannttac taaccac 177

<210> 712  
<211> 185  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(185)  
<223> n=A,T,C or G

<400> 712  
aaacgnacca nngccaacga tangtggttg ngttggttgc ggttggttct cttatntgca 60  
ctgggttgcc gtgtgcacg ganggccacg tccctctgnc ntgagtanca catagcatcc 120  
acgttttagtc gactntnccg ggcggcgcgt ctaccctnt atngattctt attaaaantc 180  
ggatc 185

<210> 713  
<211> 172  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(172)  
<223> n=A,T,C or G

<400> 713  
nntgggtcgcc tngcgcgtnta ctctaaagga tntactatnc atatggantc naanacgact 60  
cactacacgg cncctnccg agccnnggtc agtgccctnct nggagacctt ctctggggca 120  
ggangagcac tnggtatggt cagctatcnc ttcntaaana tacnnccctc cg 172

<210> 714  
<211> 112  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(714)  
<223> n=A,T,C or G

<400> 714  
nttgcggtgcc tggacgtnta ctctgcanga tctactactc atnggaattc taantacgga 60

263

ctcactatnc ggcancgcag gcgcagcagg gaanggggtca cctcccagtc tc 112

<210> 715

<211> 326

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(326)

<223> n=A,T,C or G

<400> 715

tactctanag gatctncgng tcatntggat tctatntcga ctcactctag ggctcnagcn 60  
gtcngccggg caagttattc ggatcgtcgg gntccgagct tcgcaattaa ntgtgccatc 120  
gttctncaac gttcctgact nggaancccc ngcngttcng atccnonggt acctagctcc 180  
anntcccccg tntccttctt ggngtntcat naangaggac cncctcgcg cnccttctc 240  
taatctgcnc acnctgaacg nccaatggac atngtgcggt taatntanna ggcccgnttc 300  
ngtgcctt cccgtnannt cagctc 326

<210> 716

<211> 122

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(122)

<223> n=A,T,C or G

<400> 716

nntgcgtgc ctgngcgtnt actctagatg atctgantag tcatatggat tctaatacga 60  
ctcannatag ggctctagcg nggatncnga ttogtontcc ngattcantg acnccgggtan 120  
ca 122

<210> 717

<211> 203

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(203)

<223> n=A,T,C or G

<400> 717

cntgcatgcc tgcaggtcga ctctagagga totactagtc atatggatcg agcggccgcc 60  
cgggcagggtg tnaatgataa anatgcatca tactanccta cagaanggag agataatgtt 120  
ngntggacca ngttggtttt ctgctgtgtg tgtggcagta gtaagttatt agtttttana 180  
atcantaccg cctccgcac cac 203

<210> 718

<211> 168

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature



264

<222> (1)...(168)  
 <223> n=A,T,C or G

<400> 718  
 ggcagganga tcncttgagc ccngagggtc gaggtacag tgagccanga gtgcactact 60  
 gtnncgccct ccgcatncac gngtggtccg atccccgggt accganctng anttcaactgg 120  
 antttttttt aancgtnttg antggtacna cctcgcantc cctggctg 168

<210> 719  
 <211> 210  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(210)  
 <223> n=A,T,C or G

<400> 719  
 cancgctcgc ataacacgta tttntgatn aagattctna ctgacccatn aantctacnt 60  
 ctcaagctct tncanngtcc agtnaangga atgtgtatnn gtngggatnc cacanaaaaa 120  
 aganatntcg gncgcttcat tantcatcct tcttaccan ntctctngat ncncaagtntg 180  
 ancntgaacg cacactacng gatntctcca 210

<210> 720  
 <211> 131  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(131)  
 <223> n=A,T,C or G

<400> 720  
 tccatcctaa tacgactcac tatagggtcg ccaacctgcc atccactact gaggaagacc 60  
 cgnaacttta ggggtcact gcgagccacc ggccacaggt cgtatagggc aaagcacgng 120  
 gaagcaccct t 131

<210> 721  
 <211> 121  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(121)  
 <223> n=A,T,C or G

<400> 721  
 tccatcctaa tacgactcac tatagggtcg ntgantnctg gcgaaaggct tacaattaag 60  
 naggaaaaan ganccaacaa ctaaaaaaaa nncggnctg ncagcttnga tgactngtcc 120  
 a 121

<210> 722  
 <211> 246  
 <212> DNA  
 <213> Homo sapiens

265

<220>  
<221> misc\_feature  
<222> (1)...(246)  
<223> n=A,T,C or G

<400> 722  
anctggagtc ggcgcgtgca gtcacattgt ggatccanaa aatcggcaca agctctcntg 60  
gnttcntcga tatgaanaac actaatccca tgtngtntgn gtctccgtga ttcattccctc 120  
gcacnggtcc cnttcnaac cnttgcatag gtgttatgtt gtantctccc cagtgcacaa 180  
agattnacac tctctcantg tctganatat gcacgagttc attgtcctgt cnccgtnaac 240  
atcaag 246

<210> 723  
<211> 160  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(160)  
<223> n=A,T,C or G

<400> 723  
cctccggaaa atccaantag agtaantncn ctctaataccg gggnaattgg nggggttnnat 60  
acgtcctcct cccccagnt aggattnana aaaggncctcc cagancaaaa nctccaaagt 120  
gnatcnanta gccgtncceg anatincaacg cccctacgtc 160

<210> 724  
<211> 156  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(156)  
<223> n=A,T,C or G

<400> 724  
tnanccnata tacaccaaata tctgattcta aantcccacc caagggaataa aagttgagaa 60  
gagcctttcc actttttctac taataaaaaa atgcaccagc cctaccann agtgnggaaa 120  
acctccttag gcccttgnnt ggaacaancg aaaatc 156

<210> 725  
<211> 347  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(347)  
<223> n=A,T,C or G

<400> 725  
aganggttnt atncaatgctg tactcgcgcg cctgcagtcg acactagtgg atccaaagaa 60  
ttcggcacga gagacggtgc gcgatggacc gagggcccca gccgngagg cgccgccgcc 120  
gagcccgccg ncagacgccc catcagtagc gtccgcaccg ggnagccgcg gntctcgccc 180  
gagccgtggg cgcgcccagag gggcgggctc gcctcccgcc gtccctcgca gctctgccg 240

266

gccccagccc ggcgcgtcgc cgccgccgnc ttgccgctcg gncgcgcggg nccggnaaac 300  
gcggtcgagg tctggatgng gcanngcccg cncctntcgc tgagcct 347

<210> 726  
<211> 162  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(162)  
<223> n=A,T,C or G

<400> 726  
ttgggtgggt tgggtggggg naaatttncc catttgggtg ggtttggggg ggnaaataact 60  
tcccgcccttt tnggtnccca aaganacnaa gggggagtcc cttnatagag gnagncgat 120  
nntcncaac nactngact ttgnccatgg ggagnaaggt gg 162

<210> 727  
<211> 120  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(120)  
<223> n=A,T,C or G

<400> 727  
gtgtgggtgg ggaattccat tgtggttggg ggnaaatctc cgcttgtcca aagnacaggg 60  
ggggtcnctt anagnnagg ggttctctcc ccaccacttg ncttgnccat tngagnaag 120

<210> 728  
<211> 130  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(130)  
<223> n=A,T,C or G

<400> 728  
gaccactgc agcgttnaac ttagcttggg ccgagctcgg atccctagtc cgtgtggtgg 60  
aattccatgt gtcgagagag gggcaaatac nctccaanac ancncctca tgctcnacac 120  
atattcgcat 130

<210> 729  
<211> 182  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(182)  
<223> n=A,T,C or G

<400> 729

267

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cngactgctn gcgttttaaac ttaagcnagg taccgaacgg ggatnnacga ctantgatcg 60
gctggctgct tccagtcgat tanatttgtg aaaaagctga accncngccn gttaaggggg 120
annatgcaaa anantcatcc nnctgccccn taaactgntc tntccnaggg aaaaaangga 180
ag 182

```

```

<210> 730
<211> 678
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(678)
<223> n=A,T,C or G

```

```

<400> 730
cactcncact ccggacctag gcnccttcacc actgctctct tcctcctcct cctcctcctc 60
ctcggggctg ggggaccttc cccagtgacc atctcacttt ggetgaancc cactcggggc 120
agcctgagtt tggggctctt ggcccttctca cctcctcctg cccctcctt ggcccgacc 180
aggccaaacc ggggcagccg taccttgagc ttgtgtccgg cctctccctc cccctctgcc 240
acctgttact cggcatggtt gcccccgga tggcgagagc tccacgtcgg gcagtgagaa 300
gcagaaagta cgctcggccc ctgggggctg ctctcagca ccctcgcccc ccaccctagc 360
tctggcccc agtgtgggca acttcagcct cagcccaccc tcgctgtgg ccgctctgcc 420
cgctgtgcc tctcggtta gccccacgtc caactcaagc tggggcactg tcacggtggg 480
catcttaaa acaccctcac ccaccagcag ctcaccacct gcaacctggg ctccaggcaa 540
aaaaagggtc acctggggca nctgaaccct gtacctgtg tgccctctgc tgaanggaat 600
gttatctgaa cctgctgcc tgggggtact gccttcccaa aaccgggtca antccacctg 660
ttggaagga aatncccc 678

```

```

<210> 731
<211> 135
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(135)
<223> n=A,T,C or G

```

```

<400> 731
gagatccgac gtcacccctt tccggcggcc caagacgctg caactcccga ggcnegccaa 60
atatctttgg aagagcgtc ccagcccaac acaatggaat tccaccacac tggnttagtg 120
gatccgagct aagcc 135

```

```

<210> 732
<211> 660
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(660)
<223> n=A,T,C or G

```

```

<400> 732
gcttggtacc gagctnggat ccctagtaac ggccgccagt gtgctggaat tcggctttct 60
tcaatcagnt nacgagctgc atggtctgct aacattgtca taattgctgg catagattac 120
tgaaaataaa gaaaaaaaat tgaagctgcc tatcaagttt tggattatc aaaaacttcc 180

```

268

```

tacaagttat tttacttcaa ccatgttatt acaaatatatt taatgaatac ttttagagact 240
ttaattacaa aaaactgaga tagtaaaagc aagtaataaa agctgaaatt acttagctat 300
ttgataatta cataaattat tatggtccat tcaacttttc tagtgtttag tttatacacc 360
aggaagactt tcctattcta ctaacattta taaagtatgc taacctatta tttaaacgca 420
tccactatta ggattttatg gcctaaaacg tgatacagtt cagtatcttg atgtcaaaac 480
tttttaagca agtagggatt aagttcaagt gaatgtgatt ttctttcttc ccagtagggg 540
cttctgaata actcagnaac gctcacttcc attatcttac tttataaaaa aatgctataa 600
gacagaatgg gccgacgtgg nggctocacc tgtatocacc tttggaggcg agnggcgaat 660

```

&lt;210&gt; 733

&lt;211&gt; 836

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(836)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 733

```

aattaatgac tttttttccg ccctgccaaag ctagtttgtc taaatataat gtaaagaaat 60
tagctactca ttttctgggc cacgaagggt cctaaaatgg gaagaagtgg agatctgacc 120
ttgttagttc taaatacact aaactgggag tgccatggat ggctttcagg atgtcctgaa 180
tcctctataa ttgtatacaa aatcgtgagt ttttaaaaac tgggttagag ctattgggtc 240
ctcagagtct caggcatctt agacccccc aaaggttaag gactactgac ttaaccaatt 300
aggtttgagt ggcattggct ttgaagaaa gcagaggaaa gatataattt ataattctgg 360
gcaacaaaaa agtggatgtg tgccagcatc ttagagtaga atcctcttaa aaggatagca 420
ctgcatatga actagtaggt ttaaccagt gcatatttag gcgaagtagc tcatttttct 480
gttagaattc ttttttattt gggaatgggc aagcttttac agcttttacc ttgccaatga 540
atacctggaa tttaaaaaat ctgtgtaggc atattgcccc taaagttttt tttcctagat 600
catatattca gtaaatatgt ttgtagcttt atttcaatcc cccaattcat tgagggttga 660
aacaatttga atggtttgag tgtagaagct aagttatttc tgtagaggct aagggcattt 720
ataccaanat atgttagact tngngntcct gtaaccatg ctgtanacaa taggaattac 780
tgtatatcca cattttaatt ttaacatctt ctgctttgnt gntgggttga gangga 836

```

&lt;210&gt; 734

&lt;211&gt; 694

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(694)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 734

```

nagtnctatt tncactaaac tngnagtgcc ttggatggct ttcaggatgt cctgaatcct 60
ctataattgt atacaaaatc gtgagttttt aaaaactggg ttagagctat tggttcctca 120
gagtctcagg catcttagac ccccaaaaag gttaaggact actgacttaa ccaattagg 180
ttgagtggca ttggctttga agaaaagcag aggaaagata tattttataa ttctgggcaa 240
caaaaaagtg gatgtgtgcc agcatcttag agtagaatcc tcttaaaagg atagcactgc 300
atatgaacta gtaggtttta accagtgcac atttaggcga agtagctcat ttttctgtta 360
gaattctttt ttatttggga atgggcaagc ttttacagct tttacottgc caatgaatac 420
ctggaattta aaaaatcttg ttaggcataat tgcccataaa gtttttttct ctagatcata 480
tattcagtaa atatgtttgt agcttttatt caatcccca attcattgag ggttgaaaca 540
atttgaatgg tttgagtgtg gaagctaagt tatttctgta gaggctaagg gcatttatac 600
caagatatgt tagacttgtg gttcctgtta accattgctg tagacaatag gaattactgt 660
atatccacat ttttaatttt aacatcattc tgctc 694

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269

<210> 735  
<211> 126  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(126)  
<223> n=A,T,C or G

<400> 735  
ncnttgaaac nggttgacca gacttcaggc ctgtgcgctc aatcgtggag aatctcgtgc 60  
cgaattcggc acgagtctct ctctctctct ctctctctct ctctctctct ntctctctct 120  
ctctct 126

<210> 736  
<211> 165  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(165)  
<223> n=A,T,C or G

<400> 736  
cagaagcctt taaaccggtt ngaccagact tcaggcctgt gcgctcaatc gtggagaatc 60  
tcgtgccgaa ttcggcacga gtctctctct ctctctctct ctctctctct ctctctctct 120  
ctctctctct ctctctctct ctctctctct ctctctctct ctctc 165

<210> 737  
<211> 125  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(125)  
<223> n=A,T,C or G

<400> 737  
ggnagccctt ttaaccgttt gtccagactt caggcctgtg cgctcaatcg tggagaatct 60  
cgtgccgaat tcggcacgag tctctctctc tctctctctc tctctctctc tctctntctc 120  
tctct 125

<210> 738  
<211> 137  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(137)  
<223> n=A,T,C or G

<400> 738

270

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ggagnncnctt gancaggatg accgacttca ggcctgtgcg ctcaatcgtg gagaatctcg 60
tgccgaattc ggcacgagtc tctctctctc tctctctctc tctctctctc tctctctctc 120
tctctctctc tctctctc                                     137

```

```

<210> 739
<211> 970
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(970)
<223> n=A,T,C or G

```

```

<400> 739
aggcctatatt aggtgacact atagaacaag tttgtacaaa aaagcaggct ggtaccgggtc 60
cggaattcgc gccgcgctcg acggcccttn gtgccactag ntctttcatt cttccccccc 120
atcaatcagt gaacttttta gcctactcaa agctttgtct caatgcatag gatttatgat 180
tgtggggatt tccagataat ataaatattc aacatgaata ttttaaatta aggcatagaga 240
catttttctt aactgagcat agccatgaac ctctcacgtc tggtcctctg tgtcagtttg 300
tancactgaa tacagcagcc ctccataaaag tccaggcagt gcacaggctc tgacatgatg 360
aagtgcgctg ttgctatggt gattttgcag ctggccaaat agtcactggt tgattttacc 420
cagcaggaga tttttgcaaa aatttcctgg gtgagagtga aatcaaactc ctattttgnt 480
tctcctctgc aagctgnagt taagatggat taatgagtag ttttagatta attaactctg 540
aagagaaaaa gggagaaaaa tgaggaaagt tgttggcaga agtcattgct ggaatccttc 600
tgaagggagt actgacttca cttgcaaaga cnagagacta naagacaatg aagttaaact 660
tggcctgtct ctcatatgat agatgctgag agtcaggntc agggaaattt aattctgtca 720
tagcatatn ggattatgtg gtcattggatt tgttggcact aaccngcctn taatcagnat 780
aagaaaagtg ttttggtaga naaagaaaaa tatggcccag aaaaacctgg aanacttgga 840
aaaaatgntn gggggccttg ggtggtggtc tnaaaanacc ccctggggat ntttaaacca 900
aaantgaaga agggaaaaa ntttccccnt nttttntttt tttgccccct tgggattggn 960
ttttntttcc                                     970

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```

<210> 740
<211> 739
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(739)
<223> n=A,T,C or G

```

```

<400> 740
gntgtcnaaa aagcaggctg gtaccgggtc ggaattcgcg gccgcgtcga cggcccttgg 60
tgccactagt tctttcattc ttccccncca tcaatcagtg aacttttttag cctactcaaa 120
gctttgctcc aatgcatagg atttatgatt gtggggattt ccagataata taaatattca 180
acatgaatat tttaaattaa ggcagtagac atttttccta actgagcata gccatgaacc 240
tctcagctct gttcctctgt gncagtttgt agcactgaat acagcagccc tcctaaaagt 300
ccaggcagtg cacaggctct gacatgatga agtgacgtgt tgctatggtg attttgtagc 360
tggccaaata gtcactggtt gatttttacc agcaggagat ttttgcaaaa atttcctggg 420
tgagagtga atcaaactcc tattttggtt ctccctctgca agctgnagtt aanatggatt 480
aatgagtact ttttagattaa ttaactctga agagaaaatg ggagaaaagn gaggaagggt 540
gttggcagaa gtcattgctg gaatccttct gaagggagta ctgacttcac ttgcaaagac 600
aagagactan aagacaatga agttaaactt ggcctgtctn tcatatgata gatgcttgag 660
agtacaggnt cagggaat ttaattctgn catacgcata ttggattatg tgggtcatgg 720
ctttgtttgg cncctaacc                                     739

```

271

<210> 741  
 <211> 1171  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(1171)  
 <223> n=A,T,C or G

<400> 741:  
 gccttgnggt gacactatag aacatgtttg tacaaaaaag caggctggta ccggtccgga 60  
 attcgcgggc gcgtcgacgg cccttnntgc cactagtctt ttcatctctc ccccccacatca 120  
 atcagtgaac ttttttagcct actcaaagct ttgctccaat gcataggatt tatgattgtg 180  
 gggatttcca gataatataa atattcaaca tgaatatatt aaattaaggc atgagacatt 240  
 tttcctaact gagcatagcc atgaacctct cacgtctgtt cctctgtgtc agtttgtagc 300  
 actgaatata gcagccctcc taaaagtcca ggcagtgcac aggtcttgac atgatgaagt 360  
 gacgtgttgc tatgtgtgatt ttgcagctgg ccaaatagtc actggttgat tttaccagc 420  
 aggagatttt tgcaaaaatt tcctgggtga gagtgaatc aaactcctat ttgtttctc 480  
 ctctgcaagc tgtagttaag aagggtataa tggagtactt tttagaatt aaattaacct 540  
 cttgaaagaa gaaaaaatgg gggaagaaaa aaagtgaag ggaaaaggn ttggttttgg 600  
 gccnaaaaaa aagttccaan tttnngcctt ggggaaaaat tcccctttt ccttggnaaa 660  
 aggggggnaa ggttaancct tgggaacctt tttccnncct tttnngccca aaaggggaac 720  
 ccanggggaa agaaccttta ggnaaaggaa acccatttgg gaanggggtt naaaacctt 780  
 ngggcccccg ggcctcctc caanaaggga aaaaaaaagg cctggaaaan gtaccagggt 840  
 ttcangggna aaanttaaaa ttcttggcca atancccat aattgggaat tatggggggg 900  
 ccatgggctt ttggttttgg cncctaaccc cgcnttttaa attcaaanna aaaaaagng 960  
 gtttggaaaa nnaaaanaaaa aaaattnaan ggncccnaaa aaaaacctg gaaaacctt 1020  
 ggaaaaaaat tngnnggggg gccnttttgt tgggggggtt tnaaaaaacc ccctnggggg 1080  
 ttttttaagc ccaaaagggg gggaggggna aaanggtnc cttntttttt ttttnngccc 1140  
 cccttgggga atggnntant tcanggggcc c 1171

<210> 742  
 <211> 739  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(739)  
 <223> n=A,T,C or G

<400> 742  
 gntgtcnaaa aagcaggctg gtaccggctc ggaattcgcg gcgcgctcga cggcccttgg 60  
 tgccactagt tctttcattc ttcccnccca tcaatcagt aactttttag cctactcaaa 120  
 gctttgctcc aatgcatagg atttatgatt gtggggattt ccagataata taaatattca 180  
 acatgaatat tttaaattaa ggcataagac attttcccta actgagcata gccatgaacc 240  
 tctcacgtct gttcctctgt gncagtttgt agcactgaat acagcagccc tctaaaaagt 300  
 ccaggcagtg cacaggctct gacatgatga agtgacgtgt tgctatggtg attttgcagc 360  
 tggccaaata gtcactggtt gattttaccc agcaggagat ttttgcaaaa atttcttggg 420  
 tgagagtga atcaaaactc tattttgttt ctctctgca agctgnagt aaataggatt 480  
 aatgagtact ttttagattaa ttaactctga agagaaaatg ggagaaaagn gaggaaggtt 540  
 gttggcagaa gtcattgctg gaatccttct gaaggagta ctgacttcac ttgcaaagac 600  
 aagagactan aagacaatga agttaactt ggcctgtctn tcatatgata gatgcttgag 660  
 agtacaggnt cagggaattt ttaattctgn catacgcata ttggattatg tgggtcatgg 720  
 ctttgtttgg cncctaacc 739



272

<210> 743  
<211> 610  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(610)  
<223> n=A,T,C or G

<400> 743  
ctgtccttat ttcttttagca aaaatttccc aagagaagaa ttgctgggat aatgcacatt 60  
taaatttttg atagacattc ccaaataatta tacctgtttt tgagaccttt aattcctgtt 120  
gtcaaattgc cctatatatg gagtaataaa cacgatttaa agaaatgagg actaaaaaaaa 180  
gattatatat aacccaacat aaaggcaacc tcttaggcgt tgacagaaac tgacaacttt 240  
ttatctgtgg gtgcgatcca ttataagtaa cctgagcacc ttattttttc tttttaaact 300  
ctaggtagga taccogaggt ccacaattt ttcataagaa atattttttc tctgccctat 360  
gagattttta aaaatattat actgcttcaa ttgcatcaaa agaaatggac cctaatatct 420  
atgatgaagg atttggagtt agaagacctg agtttcaatt ttggcatggc tgtttgtcta 480  
gctctgngat cttggacagg tcaattgact tggcttaatc ttctcatcca tttagnngag 540  
acagcaccac tattcacagg actattgncn gaattaccag acaatagcat agngaaaaat 600  
ataangcctt 610

<210> 744  
<211> 127  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(127)  
<223> n=A,T,C or G

<400> 744  
ttnacctccc tggaccgggc ccccttccc cgggcggntc ccccgggctg caggaattct 60  
gcacgaggga gagagagttt gagagagaga gagagagaga gagagagaga gagananaga 120  
gagagag 127

<210> 745  
<211> 458  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(458)  
<223> n=A,T,C or G

<400> 745  
gatatcccgg gattcgcggc cgcgtcgacg tggcctctag tttgtcctgg tccaaagcag 60  
ggaagctggg ctacgtcctg cccaggctcag ccttaggtta agggctgcct gggggaggga 120  
acttctctgg ccttcgggtc tctgtgcact ggggtggctc ctgtggccca gaatgccctg 180  
gagaaggggt ctaactggaag cgaagggtga gggcagcagg gcctgaggcg caggagctgg 240  
tggaggctcc cagcacaggt cgccgcccc gtcacatcac tgctgatggt ggggggactt 300  
ggggagtttc ccccgagaat gggagggtctc acagtccccg tgctgcaatg ctgtcgggtgc 360  
actgngncng caatgtgctc atggnacatt gctttttctc tgtggccccg gccgatttat 420  
ccagcanngc acccctcttc tncctctccg anaaagcc 458

273

<210> 746  
 <211> 893  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(893)  
 <223> n=A,T,C or G

<400> 746  
 aagcaggctg gtaccggtcc ggaattcgcg gccgcgtcga cgtggggagt tagctctctg 60  
 gaccccgta tagagtaagt catcgataga gcatttgctt gatggggact tccagaaggc 120  
 canngaaagt cctgccgact tcctggggaa gcccatccgc acgtgggggtg aggggtcccca 180  
 natggaagca gctgtgtatg caggaggggg gcagaggctg ctgccaatgg gcatgtccct 240  
 tacctgaaag ggccacactc ccaggtgaca tgtcctgggg gagccggggc cgtctgctcc 300  
 ggccagaggc gctcagctca ggccacacca ggcaggggcac ctcccaacct ggacagggtg 360  
 ggaccaaggt ggccttgagc aaaactctct gtgtttgcc aagcaccat cggacacaga 420  
 gagtcaacca caccacagtc acatggtgtc cacacngcag ggggtcaagga ggcccgggcc 480  
 ctccccctca gacgtccctg ggccctctgg agtcagcaag gacgaggacg gcattgccct 540  
 tcgagacagg aagggagtga cctcctcccg ggggcatcca ggctcngctt ctccggagag 600  
 gagagggggc tacttgctgg ataaancggc cggggccaca gagaaaaagc aaggtgacca 660  
 tgagcacctt gcaaacacag tgcaccacc agcatttnag caccngggac tgtgaagacc 720  
 tccccattct tcggggggaa acncgccaa ngttccccc accntcacta gtgnattgtg 780  
 acctgggggn cgggcccagc cctgtngctt gggnnagccc tccnccagc tttctnnggc 840  
 ngcccnttaa nggncctng nttggccctt tggcncctt tncgcttttc cca 893

<210> 747  
 <211> 738  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(738)  
 <223> n=A,T,C or G

<400> 747  
 gatatcccgg gaattcgcgg ccgcgtcnao gaagcacaga cctgngccct gctctcatgg 60  
 ggcagactgc catttgtcat tnattactga aggaaaggga tcctcagttt gcttgtggac 120  
 atttcaaatt tgaggtgaga gttggataag taagaataaa gctgctcttc aaagagatga 180  
 atatagaaaa agaaacaaga tacagncttg gcagtaaggc tgggaggaag gggaaaagg 240  
 aataaagaat gaaagagtga gaaatgtgag caggagctga acacagaaaa gttcagngac 300  
 agaagcanaa ggagggaaga agggaggagg gtccttttca cagaggctca cgaggatgct 360  
 ttatgngtgc catgcagtc atgttcagga tgtctgcttc ttanctctct acttttctaa 420  
 tanaaatttg gatacttact gatcctacat atgtaacagg gagagaagg gaatttcaaa 480  
 gcantaaatt gaaaaattgt tcacaatttc attttttaaa aaaaggagc taacagaaga 540  
 agaggttaat gtggtaatta taggatgnc cttgcgacac atgaatgnat ctggtatcat 600  
 ctgagtgggg ggggagctgt cttcctgacc caaaaggatc ctttcgttan ccngnactta 660  
 ngtcccaaaa cctcaccacc ttggagaaat natttccttt tgggggtntc attaaancct 720  
 tttggncccc gcaaaagc 738

<210> 748  
 <211> 647  
 <212> DNA  
 <213> Homo sapiens

<220>

274

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(647)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 748

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ctntgtggcg gtggctgtct catttgggtg gacttttttg gtcgtaggaa cctggtatng 60
aggtcgagag taagacgggc tattagtagt cgcacgagag ttatttgtga aaacctggtt 120
agggcctctg tctccgctgc gctcgcctaa attggtatgg ctcgacttgg aaacacggtt 180
ctaacacgcg ttgttagcgc ccttgctagc atgtgaagga cactggccct accaagaaag 240
attcgagtcg ctccctccgg tatcgttcac ggaggcgata tttactcttc ttactacggt 300
tacttcgaga ttgtctgtga agtttaagac tactaaaaag agtattaagc ctatcgggaa 360
ttagctagat cgacacgcta aaaccaaggg caatcggcgg aaatatagag gcaccaataa 420
tagggcctac agaaggcccg agggttagac tcacgtttta taccggccac gggagaaata 480
aaaagataaa gtatacatcg ttttagcggtc ctccgaagcc ttcggcttta atgccaagga 540
gtcgaagca tcgtcggcga gtaataaact ccacgcgcc gagactatct acgacgccct 600
ccttaanatc cgtaaattac tcccggaaag agtatntagc cggctct 647

```

&lt;210&gt; 749

&lt;211&gt; 642

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(642)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 749

```

ctntgtggcg gtgntgtct catttgggtg gacttttttg gtcgtaggaa cctggtatgc 60
aggtccgcgg agcgtgggct ctgcgtcgtg atgttggggg ttggtgtggt gccggttgtt 120
tttggttctg ttgagcgtag tgtgtttgaa ggttagcggt cgtgtcttgc ttgtggtttg 180
gtgttttaggg cgggtgggga ggttgttgtg tagctgttgt atgtcatatt gttggtgttg 240
ctgccctgtg ctgtttgtcc ttggttattg tggtgttac cccgcctgtg tggaagtgtt 300
gtggcagggc ggaattttaa gtgggagagt tgtgggacct gtggttgttg ttacgttgc 360
gcttttgtcg tggcggttgg cggcgcgtct gataattaga attggatacg gagtgtataa 420
tacttctagt aaatggggac ctagtgttgc acttcccgga atagggatct atgcgaagtc 480
cttaggatag tctttgataa gtttaacgcc caccacccta aaattataca cgattagacg 540
cataacgact cctccaggaa agataaagaa tctcacatat agaacgggac ccatacacg 600
tcggatagga aacaagagaa ctaattttng ttaaaaagac tt 642

```

&lt;210&gt; 750

&lt;211&gt; 639

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(639)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 750

```

tttgtggcgg tgggtgtctca tttgggtgga tttttgggtc gtaggtaacc tggtatngag 60
gtatagatgc cgattggtcc cgacgagcgt caccgataaat tcggtagttt cgcccttttt 120
agaaggcgct agtactcgga acttcacttc atctcgttag tttacttttg cgtatatagc 180
cttctccctc gaagactagc cgtcacattc gttccctagg aatcgtttct gccctaaga 240
atccagagga gagatccga aactagagga accttagaag agtcgtattt ccacaaggac 300
cccacagtca ttccgggaaa atccctagga ccatacgggt aggattcccc cggaaccggg 360
agcaaagctc atgatttccc acaccgcgag agcgcctata accctatccc atttcttcgg 420

```

275

```

gttatcgagg atattacgat caagcogaga gaaccgctag aaccgctttc ttcgctttct 480
cacggaacct ataagtagaa agagaaactc aggtcttaag gggcgcttc ggctaacgaa 540
acttctactt acgaagagag tatctagaca ttaagtcata aaaatccact acgcacctcg 600
tgtacgatat catcgggagc ggttcataga cgggtgtccg 639

```

```

<210> 751
<211> 637
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(637)
<223> n=A,T,C or G

```

```

<400> 751
cttttgtggc gngggtgtct catttgggtg gatthtttggg tegttaggnaa cctgggtatng 60
aggcagctct gagccccccc ccccccccc cccccnccc ccccccccta gngggttggg 120
aanaacgggtg atacctaaat cgagtgngtt cattaanaag agttgattac nccctaaaat 180
aanaanaggg cttcgtcggg anaaatcggg aagganaagt cttnttggca tcataanaat 240
actggctcgg gtcctaanaat nttaaggng gtcnccgagg gtnttcatac cgataanaaa 300
cgttttccta tcggcaacgg gcttacctga gggnggactt ctncggngc gnggattnan 360
acgaanacgt agaggattnc cgntacttnt tganatcacn cgtatcatac ttgtaagcat 420
aatnttctctg aaaagtgtta taanaatacg cncgcataatt cgctttttcg tcctagggat 480
gcttaaatgg cgatactgct atagcgggtg agcgttgggt ctcgagnaan aaagcgtgtc 540
ctaatacgctc taaggnttta agnccgttgg tttaaaaata nccctagaaa cctcgaggcg 600
gatactggtt tntttttaac gaaacaaagc accccnn 637

```

```

<210> 752
<211> 644
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(644)
<223> n=A,T,C or G

```

```

<400> 752
tntgtggcgg tgggtgctcat ttgggtggat ttttgggtcg taggaacctg gtatgaggtc 60
ttgcgagttg ttggtgtgtc ctgtcgttcg gtggttccct tttgagttga gtttgtcctt 120
tgaggttgtt agctgctgtt cgtttgtgtt cgtgtagtgc tttgggttga gagggttatg 180
gtggtgggta cgggtgtattg tcgcccggtg tcgcggggtt ggggtggtcg tcggttttgt 240
ggttcatagt agtcttctgc gttcggtggt gcgggttttg gtgagtagtt tcgttcttgg 300
atgtccatt gaccgcccat aatctaagta agggttagta gaaacctctc cccgatagac 360
acaaccgtcg tccactaaag acctcgctc tgatttttaa aaggacccga aaaacatccc 420
ttcaacggaa aaaacggaaa aaaagtcagc gaattcaaag aagccacggg agagaaaaaa 480
gaactaaagt tagtccgtca ttatatgtct cctcggagga ggaagcggcg gtggcggaaa 540
atgaggcggg aagaaagacg acctctatcg gcggcctang ccctaaaagg gcgatacctt 600
acgggatgat aaggacccta ggacgcctcc ttctcgatc gtcc 644

```

```

<210> 753
<211> 635
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature

```

276

&lt;222&gt; (1)...(635)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 753

```

ctttgtggcg gtgggtgctca tttgggtgga tttttgggtc gtaggaacct ggtatgaggg 60
aatcagctcg accccccccc cccccccct ccgaagcaga gcccaacca aagtccaccg 120
actaccgag taaactctcg gagggtagaa taagaaggag taggtcctag ccaatagaag 180
tagttccgag cgttaggac agcggacgga acattnaaga aagagcctat attagggagg 240
aagtaacgtt cctctttcgg agctctttaa ggggtagtcc cagaacaagg gaagaggacc 300
cgtcggctat tgcccgtcga tacgggctct cacggngagc ctaggttcga ggatagggcc 360
gctcgtaaaa ttatacggtt tccgagaaac gcttccgtag accgggtcct aaatcgtccg 420
gagtattngg agaggggatcc ttcggaccct agggacagag agaggagaac ggaggttaca 480
ggaggagaac gtntcctcnc tagttttctt tangtcgaaa aatttcottac cgataggggt 540
cctagggctg gngaatttac ggttcgaaaa acggtagtnc ctaanggntg ntattngggg 600
tagtatcggg tcgtttacaa ntcgtccgtc ttntg 635

```

&lt;210&gt; 754

&lt;211&gt; 721

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(721)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 754

```

accggattng ttncgtgagcg cgtgactgct aataaaaaag atggantgcc atcttttttt 60
ttnccttgct ttatatatcc agcagcaaaa caaaattggt ctgcngggct ataaaatttg 120
gcttgtagt cntgtacaca actcaggagt gtgacacagc taccagcttt cctcctaact 180
ctcaaggga gaaaattcaa gttctgtcta ggctcactct gtaaagtggg aaacttgctg 240
gttttgtagg ctttttttcc ccttctttcc ctctctcagc ttctccctgc ttctcagaan 300
atggagttgt gatgcctgca acttaccaaa tttatctatg aatcagattc cagtgggaga 360
ccctaagc agaggagaa taaggagttc tcccctgat ggaaaatc caaagacaag 420
gtttcatgga gcaagaatt ctggctagat ttggtttgta agtggatccc tccccactgc 480
gtgtacactt tatctgtctc ttgtcttctt cccaccctc ttccctcagc ctctctctgt 540
ctctctcttg ntcccctgac ccttttttct tcccantgca tacttttttn ttccctttt 600
ttaatcttct atantcttaa nctaccaan gggccctcnt gannaatttn tccccctga 660
ataggggatt cnttangccc tgagaatttc nttatcanaa aaatatattt ttaaagcatt 720
a 721

```

&lt;210&gt; 755

&lt;211&gt; 721

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(721)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 755

```

accggattng ttncgtgagcg cgtgactgct aataaaaaag atggantgcc atcttttttt 60
ttnccttgct ttatatatcc agcagcaaaa caaaattggt ctgcngggct ataaaatttg 120
gcttgtagt cntgtacaca actcaggagt gtgacacagc taccagcttt cctcctaact 180
ctcaaggga gaaaattcaa gttctgtcta ggctcactct gtaaagtggg aaacttgctg 240
gttttgtagg ctttttttcc ccttctttcc ctctctcagc ttctccctgc ttctcagaan 300
atggagttgt gatgcctgca acttaccaaa tttatctatg aatcagattc cagtgggaga 360

```

277

```

ccccataaagc agagggagaa taaggagttc tccccatgat ggaaaatata caaagacaag 420
gtttcatgga gcaaagaatt ctggctagat ttggtttgta agtggatccc tccccactgc 480
gtgtacactt tatctgtctc ttgtcttctt cccaccctc tttcccagct ctctctctgt 540
ctctctcttg ntcccctgac ccttttttct tcccantgca tacttttttn tttccctttt 600
ttaatcttct atantcttaa ncctaccaan ggccctctent gannaatttn tcaccctga 660
ataggggatt ctntangccc tgagaatttc nttatcanaa aaatatTTTT ttaaagcatt 720
a 721

```

&lt;210&gt; 756

&lt;211&gt; 873

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(873)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 756

```

ggaagaatac agtaagtttg caaattaaaa tttctctatt tttctgttat ttattcattt 60
ggaaactgtc agcctgtctc tttcactttg ggcaagtga agcaaagacg tccagtccta 120
tcagcaatta ggctgaaagt caacgccaag ctggcgggca agggctggtc tgagtagagg 180
ttccctaggc aggcaagaga gagactcca ctcgatactc ccagctcggc aactgcctga 240
atgccaatga gcactcatta taaccggccc tattttatag gatttaattt tacacttcag 300
gcttaatcag tctgaaagt aaactgacag tgttaagtta cggaatcaat gacatttagg 360
ctttatgact ttgtagctga atatctatgg gctatatttc cattctaaca gtgatattcct 420
gttccagaat ctcatctttt ggtgatggca ctttctagtg gagcagtcac ggtaacagtc 480
cacacccatt accatgtggg tgctttacag catactgacg gaaggactga ggagccaccg 540
gagcaggagt tctctcaggg gaggacgctg acacttcac agctgcctan gtatgggcac 600
ctgatgccaa cgaanaaccc aaagcgctct ccctccaga tggagctgc cccacactgg 660
gctgacagca tctggagctg ctctggctca aatccggaa tcgcacanct octancgggg 720
gcgtttanag atcctcnggg ccagctaccg accacttttg acaagggncct taggagcgat 780
aactagnctg gcgcgttaca cncggatgga acgtcttgga cttgagacct cttgggggan 840
atggcncccc caaataantt gggaaaaantn ggg 873

```

&lt;210&gt; 757

&lt;211&gt; 782

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(782)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 757

```

ggccctcga gggatactct agagcgcccg ccgactagt agctcgtcga cgatatcccg 60
ggatttgaga ccaggagaca gctccagatg ctgtcagccc agtgctgggg gcaggcttcc 120
atctgtgaag tggagaggcg ctttgggctt ctctgtggc atcaggtgcc catacctagg 180
gcagctgtgg aagtgtcagc gtcctccctg agaggaaactc ctgctccggg ggctcctcag 240
tccttccgtc agtatgtgt aaagcaccca catggtaatg ggtgnggact ggtaccatga 300
ctgntccctt aaaagtggtg cttcccaag aaaggagaat tcttggaacna gggatttcac 360
ttgnttagaa atgggaaaaa ttaccattta gaattttcgn ttccaaggcn tnaagncccta 420
aaaggccttt gattcccgaa ccttaaccct gggcagttta cctttcaaac gggataaacc 480
ctgangggga aatnaaatc ctttaaaaaa gggggggttt naaggagggc tctttggctt 540
tcaggcantt gccaacctgg gaaattcana ggggaagtnt ttttttttgc ctgcctaggg 600
aacctttact taaacnaacc cttgnccccc catttggggg tgactttcan cctaattgct 660
gaaaggaccg ggccgntttt gntttccttt gncccaaagg naaanaaacg ggtgccantt 720

```

278

cccangggat tanttcccgga aaatttgggn aatttttntt tgnaactttt tgggtttttt 780  
cc 782

<210> 758  
<211> 647  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(647)  
<223> n=A,T,C or G

<400> 758  
ntttgtggcg gtggtgtctc atttgggtgg actttttggg tcgtaggaac ctggtatnga 60  
gggaagagcg ccgtcgggtcc gaggtagta tagtcttcgc gccttctcgg 120  
gcggcggggc tattctctcc aaaggcagag gtccctagtc gacctcgtc ccctagggtta 180  
ggaacagccg tcgaatattt taggttcgtc gaggctttct tccgagctct acgcctaagt 240  
agctccgcga gcaaaagtac ggtcattttc ccctatccat cactcccta agtacgcctc 300  
attattccgg aaggcaagag gccagcattc ctccttagag tagagggtag gtacctccgt 360  
cgctgcgcg gaaagggcag agcttcgtgt cttccctccg cagcagctta acggtctacg 420  
taggcgttct cgatcttttc acgggaatcg gggtcgggga gggcggcgga aaacgtcgac 480  
gtctcgggtca ccgtcaccgc cccgaacaac tagcggcttt ccgctttcaa ctgagggaacc 540  
ccgcacccct cattagcgct tacgaaatcg gggangtgat tgcgccaatt cgtagcctt 600  
cgataaattat tctctattag cggtcctatc tcgcgctttc gatttat 647

<210> 759  
<211> 657  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(657)  
<223> n=A,T,C or G

<400> 759  
ctttgtggcg gtggtgtctc atttgggtgg actttttggg tcgtaggaac ctggtatnga 60  
gggctctata gaaagcctct tgtctttaga tacgggcttt ctggtccttc gttctggaag 120  
tgtagtagta ggtactgcgg gaaggcgaag agtcctttca aggacgattt acttaagttg 180  
gcttattcta tagttccttc gggacataag gtcggtacga tctatactgc gtgggaagct 240  
gataggttgg gacttaaggc gaataagaag gaggcggcgg aggtcgcgat taccgcagag 300  
atattattta cggcggccgc gggtaaccgc ggtcatgcgg aaattttctg aggttcttgg 360  
attcctaaga tcgctcccggt cgagtatact agcgacgaac gtaagagtgc cctcacaaga 420  
accggtacaa actcaagaag aagttcccat taagcatcgt aagaaacggg aggacgagga 480  
cggtaagaag taatcggaga aaggatccta gtngttacga agaagcatcg ttnagctact 540  
ttgcgctacc gtttatattt agacgtgttc cgtccttctc cgtgtttana aaaaagggtt 600  
attccgacgg gagacttagg cgaatggagg gttccgcggg tganaatcgg ancgggg 657

<210> 760  
<211> 644  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(644)  
<223> n=A,T,C or G

279

```

<400> 760
ctttgtggcg gtggtgtctc atttgggtgg actttttggg tcgtaggaac ctggtatgna 60
ggaaaagaag taagcctcga agcctatctc cgaccgtatt tatttcgcag aagacggaac 120
tacggacgtc gttaaccccg agtagccccc gtaagaaagg actaaagcga atggaaaagt 180
cggaattcc ggcgaggagg cggcgattac tgaaaggagt aagagtaaga ctattgcgat 240
acttgaggcg ttccctctta aaaggcacc cgaacactct attaaaaaac acccgaagaa 300
gaacaactca tgcgatcggc cgtgtgcagc cgtcaatagt aaagagagcc atgaaccatg 360
ccatccttag accaattagg atgaagaaga ggaggaagat gaggaccaa ccctaccac 420
tcgaaaaacc ccgcacgagc ctccgaacaa aatccgggaa ttaaacggc ggccacttc 480
cgcactctcg tagcgcggac cgaatagaaa accggaaact acagctaaag ggtcctttcc 540
ggcctgttat ctaccaccc gcaatccgat cctccccc cctcgtccaa aaaccctaac 600
ctctgcggca acattagagc agaaggagag ggcgatccct tgan 644

```

```

<210> 761
<211> 647
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(647)
<223> n=A,T,C or G

```

```

<400> 761
ctttgtggcg gtggtgtctc atttgggtgg actttttggg tcgtaggaac ctggtatnga 60
ggcgggtact ctctgggata atcggtataa gtgtttgtaa attgggggta agagaaagt 120
tcattataag aagtggaagc acgagccggg gtgttttagtc gttaatatta agaccggtt 180
ttgtttgact tatatagctt gcgcgtgggg aggcataaag aaacattgcg ttctgaggcc 240
ggatgcgggg aaccctcttc ggggtctaga gcgcgcgcat tgcaaaataa ggactactga 300
cgccgctcat aacgtactca acaatgagtc ggcctgcatt aagatttcgg cgaagaaccg 360
tactgcgtct actgatagta tattgcattg atagcggcat gagctttatc acgtgtcgtt 420
ttcgggttgt aagaaggag ttaagtcgat ctctgaggaa gaagagacc caaataaaaa 480
atgactcaaa aaaacctaga agaaacacga cgaaaggaaa aagaacgtta aaactagtag 540
ctcttcggan gagtagcctt agtagggtaa gtcctccgtg cgtactgtcc taaggtttgg 600
atagcgcggt tgaatagacg gtcacgcgtc agaaggtaaa aancgg 647

```

```

<210> 762
<211> 628
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(628)
<223> n=A,T,C or G

```

```

<400> 762
cattgtgttg gggctactga gccactttt ttccagattt tttgtaaaat tgtttcgcat 60
tgtgttccct ttattcgctt gtattaatat ttgcgtagt gattaaacaa atacttggtg 120
ttgactgtca gtcttagagg actgactaga agtagttttc atttggggct caggaaatac 180
ctactttata tttctagcta attaggaaag tcatttttca gttaggttgg tgttttggtt 240
caggcactcg ctagctagat gacctaacat gctacttaat ttctgagtgt ttgtgtccat 300
ccctgtagga ttgttcggg gttaaatgaa atttgttata tttgtaaagc atttacctca 360
gtgccagac tgtgacagag tagattatta ggcttgctct tatttctgtg attaaattta 420
gtgtcagatt aagacctat agctacttct aaagctgctg ctgctttctt tgtttagggt 480
taggaagaaa catgctggac agtttgccaa atgagagtta catgatgtgg cttgtgggaa 540
cattctaact tggaacttgc ccatttccag gactttgnng ttcanagatt tttggggata 600

```



280

gatgtaagggttataaaaaa cngaaaac

628

&lt;210&gt; 763

&lt;211&gt; 147

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(147)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 763

cattgtgttg gggcagagat aaataattcc tctgaaaagt gttttattgg aatttcaaat 60  
gaaaagctaa ctggataact tacagcatgt ttctgccaat aatctcttan aacaggcctc 120  
ttttttttat gcacaccacc ttcnnggc 147

&lt;210&gt; 764

&lt;211&gt; 146

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(146)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 764

cattgtgttg ggtatgtttt ttgaaggcag gtggacagga tttgctgatg ggtaaatggc 60  
agagttaggg ggactgttag aacagagaaa.ganatcatgg gggtgggttt gagtctgatg 120  
nnnaactggg gccgnntgct cagtat 146

&lt;210&gt; 765

&lt;211&gt; 129

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(129)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 765

tnncgattc gntnctagcg tntacactna tgtcttggtta ccgagctcgg atccactagt 60  
ccagtgtggg nggaattcca ttgtgttggg gcaggaggng ctttgngtac ngtgcggctg 120  
nagaggcgg 129

&lt;210&gt; 766

&lt;211&gt; 175

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(175)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 766

281

```

cattgtgttg ggcctagtc gaatactttt agtaacttca gacagatctc ctcatctctt 60
tctggggctt ggnnttttctc ctttgtanaa tgatgccttt ctgtgggttt gtcattttcta 120
acattctgtg ngtgatgagg tgtatattcg anganctcta tcncanagt actct 175

```

```

<210> 767
<211> 602
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(602)
<223> n=A,T,C or G

```

```

<400> 767
nnnttttaaaa nctgtntctcc ccgcgggtggc ggccgctcta gaactagtgg atcctttcca 60
cctggtttgt tttcagtgtt taatcctatt agtatcagca ggatataggt caggatatca 120
ggtgcagaac ctgtggaatc agccaatttg gcttgctcat ttactttaat aagggtcccat 180
aatgagttag agtacaaaagt tcaagccctg ttgaggggtc gcattaaact ctcagaagta 240
tttagagtgt gccaggagcc gcgaaggctc ggttcgggtg gtggcgggaa ctgtattaga 300
gtgctaggca cggcgcgaca aagtctgtcc aacccaaaac ggtgctgagg cgttgggtgt 360
gagctccagt actcagaaaa gcctctcagc aggtactcaa cagatcctca ggggcttggg 420
ggcccagcac tggcagttag ggcatgaaag acataaaagg gcactacctg tgggtatttt 480
ctgttctcca aggaggaagt agcaaaaatt aggacgctgg aatatcctat gttgtagcaa 540
tcccagaaca actgatgctc aacaaatacc acacaaaaca aattttttaa aatttaaatct 600
ta 602

```

```

<210> 768
<211> 671
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(671)
<223> n=A,T,C or G

```

```

<400> 768
tccaccgcgg tggcggccgc tctagactag tggatccact agtccagtgt ggggtgggaat 60
tcgcggcncg cgtcgacaaa aatactgcta aagtaatat tttatagatg actatttgcc 120
ttggggccag gaaaagcagc tggagttatt cacttagtac catttttaca tactaacttt 180
gccttttcca tgcttgcttg atgcggcttg cagcactgaa gaacagtttc aattgctagc 240
caaccagaga gcatgatcaa accaaacaag ttccctgttt caggaaaaac aggttttagg 300
taactgaagg gttaccagt actgattcca caatcttctc tgtaaaanat ttctgcctat 360
tatgcagact gggcggcttt aaanntggta aaactatnaa ataccatac aatattttta 420
nggggccccn ttatnaagct tttcaggcct tcccctttcc atagcattgg tgggatacaa 480
gaaaccttta aacagcaacn agctatcnag gcccaaaagg aaagtaattn tgatttttta 540
nagattccgn aacgaaaaaa tggctgggtt caaatacnac cttcttttta aaatggnntc 600
cttattaaac nttttttttt ttttaattta ccccatgggc ntgatnttng ngcttccgcc 660
canaaaatng n 671

```

```

<210> 769
<211> 877
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature

```

&lt;222&gt; (1)...(877)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 769

```

aaagctggag ctccccgcgg tggcgccgc tctagaacta gtggatccac tagtccanng 60
ngggggaatt cgcgccgcgg tcgacctcta tacctttgnt catgcagctt cctctgactg 120
ggtttgttct tcaattggct aacccctctt ttacttaagc acaccttgaa cattccctcc 180
ttccccattt ccccgagng cccctaattg acatacttct gaataacaca ggtggtattc 240
cttccttggt ggaacctcct ggaggaagag acagatgatt aacaaatcct tccatcaacc 300
cctttgacca tgacatcaac agtgctccaa attatgggt accgtattag cctatgtcta 360
tcttgatcag aatccttacc tcggtgtatt gaaattatct atttcgtgcc tgcctcttta 420
aagtcagggt ttgccttacc tattgtctaa caccatgcag taggtaacat gcagtaggaa 480
acatggcatt aaattatttg ggttcaaadc ccagttatgg tgtgtaaatg cctaccaggc 540
cgtgaggcac ctgctaagca ggttgacgc atcatttgaa ttcacaccac ccttttgcaa 600
tagaacagat aggcaacaga ggctcatttg ggctaaagga tttgatggag gggagtgcc 660
aggattccca ccaaggcctc anggccagg tccanggacc atgtctgttg tgacaactgg 720
agtgcatttc atatcccctn ctctgngggg naaggtccct cncgnggaga acnnttaaaa 780
caatcatntc tnggggngnt aatgcttctt nccccagtg ggtncactgc ngccacgagt 840
cccancact agtcccangt ctgtcatgaa ccancec 877

```

&lt;210&gt; 770

&lt;211&gt; 874

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(874)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 770

```

ctggnetccc cgcggtggcg gccgctctag aactagtga tccactagtc cagtgtggtg 60
gaattcgcg cgcgctcgac cttttcaaag gtttaacttat ttaattatca canngcaac 120
ccgatgagta ggtaacagta ttttactgat aggtaatcta aagaaggagg ctaaataaat 180
tgcccaattt cgaacagtga gaggaagaat taggattgaa acacatatag tggcttcaga 240
atctgtaacc ctacgatgc cactactact tcttcoagaa taccctttgc ctatctattc 300
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ttttgagggt ttctcccttg ccagtttttc tatgctgggt tattcaagtc ctaagaattg 480
tgtagctatt acagaaccgc tttagcaaat gtgttcatt aatcaagggt atttataaca 540
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cctctcgtgt gtcccttttt tttagctatt tcagaagcac actggtgcaa tattttacga 660
aatgagtttc ttccctttac ctctgcatcc tctaagaaaa aatcattgnt gttttatgaa 720
natgaanatc ctgctatttc atatcttgat tggagctgct taattaaatg accattttta 780
aatttgtttt gattccnngc aaaaaagtt tntntttgga tgtagggggc tcnnaaagnc 840
caaaaccccc caaaattttt nnttggaac ccona 874

```

&lt;210&gt; 771

&lt;211&gt; 156

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(156)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 771

283

```

ttaaaaaanct ggncctccccg cggtggcgccg cgctctagaa ctagtgggac cactagtcca 60
gtgtgggtgga attcgcgccg gcgtcgaccg cgagcggtcg cccttttttt tttttttttt 120
ngtttttttg aanaattcat tgggtattta ttattc 156

```

&lt;210&gt; 772

&lt;211&gt; 586

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(586)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 772

```

ncaanctggg ctccaccgcg gtggcgcccg ctctagacta gtggatccac tagtccagtg 60
tggtggaatt cgcgcccgcg tcgatcacaa agtgctcaca agtccngnat ttattttatc 120
tccagatatg aaacttaccc ccagctatgg tcttctatct gttatttaat ttctaggcca 180
attttttcca cttgaatgtc agtattttta ttcaaagtca ccttgtccaa ataccaagtc 240
atcaacttac cctcaaatta tatcctcatt cagaaaatct acatctatta atggtagcta 300
ttttatccct gccccctgct ttttcttttt atatttaatt aatttgntca tccagcaaat 360
gcttattgag caggtattgt aggctaaaca attctanact ttaaggggac acagnttgca 420
aaacaaaatc ctgccttgna tggatactta tgnnatggng ggatacagac aatcaacata 480
atgangngca tcatatataa tggttagnan aatgataagg gnttttgga aaaaaatgca 540
cccanccaan anggattggg aagtggangg ganggtcang ggangg 586

```

&lt;210&gt; 773

&lt;211&gt; 2983

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 773

```

agagatagag tcttccctgg cattgcagga gagaatctga agggatgatg gatgcatcaa 60
aagagctgca agttctccac attgacttct tgaatcagga caacgccgtt tctcaccaca 120
catgggagtt ccaaacgagc agtcctgtgt tccggcgagg acagggtgtt cacctgcggc 180
tggtgctgaa ccagccccta caatcctacc accaactgaa actggaattc agcacagggc 240
cgaatcctag catcgccaaa cacaccctgg tgggtgctcg cccgaggacg ccctcagacc 300
actacaactg gcaggcaacc cttcaaaatg agtctggcaa agaggtcaca gtggctgtca 360
ccagttcccc caatgccatc ctgggcaagt accaactaaa cgtgaaaact ggaaaccaca 420
tccttaagtc tgaagaaaac atcctatacc ttctcttcaa cccatggtgt aaagaggaca 480
tggttttcat gcctgatgag gacgagcgca aagagtaacat cctcaatgac acgggctgcc 540
attacgtggg ggctgccaga agtatcaaat gcaaaccctg gaactttggt cagtttgaga 600
aaaatgtcct ggactgctgc atttccctgc tgactgagag ctccctcaag cccacagata 660
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agggcgtgct cattgggaat tggactgggg actatgaagg tggcacagcc ccatacaagt 780
ggacaggcag tgccccgatc ctgcagcagt actacaacac gaagcaggct gtgtgctttg 840
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cacgcagtgt gacaggcttc gattcagctc acgacacaga aaggaacctc acgggtggaca 960
cctatgtgaa tgagaatggc aagaaaatca ccagtatgac ccacgactct gtctggaatt 1020
tccatgtgtg gacggatgcc tggatgaagc gaccggatct gcccagggc tacgacggct 1080
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tgggccaaga caggcgaga gatatacct atgagtacaa gtatccagaa ggctcctctg 1380
aggagaggca ggtcatggat catgccttcc tccttctcag ttctgagagg gagcacagac 1440
gacctgtaaa agagaacttt cttcacatgt cggtaacaatc agatgatgtg ctgctgggaa 1500

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actctgttaa tttcacogtg attcttaaaa ggaagaccgc tgcctacag aatgtcaaca 1560  
 tcttgggctc ctttgaacta cagttgtaca ctggcaagaa gatggcaaaa ctgtgtgacc 1620  
 tcaataagac ctgcgagatc caaggtcaag tatcagaagt gactctgacc ttggactcca 1680  
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 accctgagtt ctctatagag ttgcctaaca caggcagaat tggccagcta cttgtctgca 1860  
 attgtatctt caagaatacc ctggccatcc ctttgactga cgtcaagttc tctttggaaa 1920  
 gcctgggcat ctctcacta cagacctctg accatgggac ggtgcagcct ggtgagacca 1980  
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 taagttccaa acaagtgaag gagattaatg ctcaagaatg tgttctcatc accaagtagc 2100  
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 gaagccacag agtctctccc tggagcagca gactatgggc agcccagtgct tggccactgc 2460  
 tgacgacctc tgagaagctg ccatactctc agcccatggg ttcaccagcc ctgaaggcac 2520  
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&lt;211&gt; 3064

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 774

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&lt;213&gt; Homo sapiens

&lt;400&gt; 775

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 Ser Gly Lys Glu Val Thr Val Ala Val Thr Ser Ser Pro Asn Ala Ile  
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288

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&lt;211&gt; 5668

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 777

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attattaaat attaaaatat cgatttatta ttaaaacccat ttataaggct ttttcataaa 4560
tgtatagcaa ataggaatta ttaacttgag cataagatat gagatacatg aacctgaact 4620
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taatcccagc tactcagaag gctgaggtac aagaattgct ggaacctggg aggcggaggt 4860
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gaatgggata gaattggaga gattatctta ctgaacacct gtagtccag ctttctctgg 5040
aagtgggtgt atttgagcag gatgtgcaca aggcaattga aatgcccata attagtttct 5100
cagctttgaa tacactataa actcagtggc tgaaggagga aatttttagaa ggaagctact 5160
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gtcctgtgta cttttgcaca actgagaatc ctgcggcttg gtttaatgag tgtgttcatg 5580
aaataaataa tggaggaatt gtcaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 5640
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa

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&lt;210&gt; 778

&lt;211&gt; 1095

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 778

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Met Arg Asn Arg Arg Asn Asp Thr Leu Asp Ser Thr Arg Thr Leu Tyr
                    5              10              15
Ser Ser Ala Ser Arg Ser Thr Asp Leu Ser Tyr Ser Glu Ser Asp Leu
                20              25              30
Val Asn Phe Ile Gln Ala Asn Phe Lys Lys Arg Glu Cys Val Phe Phe
                35              40              45
Thr Lys Asp Ser Lys Ala Thr Glu Asn Val Cys Lys Cys Gly Tyr Ala
                50              55              60
Gln Ser Gln His Met Glu Gly Thr Gln Ile Asn Gln Ser Glu Lys Trp
                65              70              75              80
Asn Tyr Lys Lys His Thr Lys Glu Phe Pro Thr Asp Ala Phe Gly Asp
                85              90              95
Ile Gln Phe Glu Thr Leu Gly Lys Lys Gly Lys Tyr Ile Arg Leu Ser
                100             105             110
Cys Asp Thr Asp Ala Glu Ile Leu Tyr Glu Leu Leu Thr Gln His Trp
                115             120             125
His Leu Lys Thr Pro Asn Leu Val Ile Ser Val Thr Gly Gly Ala Lys
                130             135             140
Asn Phe Ala Leu Lys Pro Arg Met Arg Lys Ile Phe Ser Arg Leu Ile
                145             150             155             160
Tyr Ile Ala Gln Ser Lys Gly Ala Trp Ile Leu Thr Gly Gly Thr His
                165             170             175
Tyr Gly Leu Thr Lys Tyr Ile Gly Glu Val Val Arg Asp Asn Thr Ile
                180             185             190
Ser Arg Ser Ser Glu Glu Asn Ile Val Ala Ile Gly Ile Ala Ala Trp
                195             200             205

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Gly Met Val Ser Asn Arg Asp Thr Leu Ile Arg Asn Cys Asp Ala Glu  
 210 215 220  
 Gly Tyr Phe Leu Ala Gln Tyr Leu Met Asp Asp Phe Thr Arg Asp Pro  
 225 230 235 240  
 Leu Tyr Ile Leu Asp Asn Asn His Thr His Leu Leu Leu Val Asp Asn  
 245 250 255  
 Gly Cys His Gly His Pro Thr Val Glu Ala Lys Leu Arg Asn Gln Leu  
 260 265 270  
 Glu Lys His Ile Ser Glu Arg Thr Ile Gln Asp Ser Asn Tyr Gly Gly  
 275 280 285  
 Lys Ile Pro Ile Val Cys Phe Ala Gln Gly Gly Gly Lys Glu Thr Leu  
 290 295 300  
 Lys Ala Ile Asn Thr Ser Ile Lys Asn Lys Ile Pro Cys Val Val Val  
 305 310 315 320  
 Glu Gly Ser Gly Arg Ile Ala Asp Val Ile Ala Ser Leu Val Glu Val  
 325 330 335  
 Glu Asp Ala Pro Thr Ser Ser Ala Val Lys Glu Lys Leu Val Arg Phe  
 340 345 350  
 Leu Pro Arg Thr Val Ser Arg Leu Ser Glu Glu Glu Thr Glu Ser Trp  
 355 360 365  
 Ile Lys Trp Leu Lys Glu Ile Leu Glu Cys Ser His Leu Leu Thr Val  
 370 375 380  
 Ile Lys Met Glu Glu Ala Gly Asp Glu Ile Val Ser Asn Ala Ile Ser  
 385 390 395 400  
 Tyr Ala Leu Tyr Lys Ala Phe Ser Thr Ser Glu Gln Asp Lys Asp Asn  
 405 410 415  
 Trp Asn Gly Gln Leu Lys Leu Leu Leu Glu Trp Asn Gln Leu Asp Leu  
 420 425 430  
 Ala Asn Asp Glu Ile Phe Thr Asn Asp Arg Arg Trp Glu Ser Ala Asp  
 435 440 445  
 Leu Gln Glu Val Met Phe Thr Ala Leu Ile Lys Asp Arg Pro Lys Phe  
 450 455 460  
 Val Arg Leu Phe Leu Glu Asn Gly Leu Asn Leu Arg Lys Phe Leu Thr  
 465 470 475 480  
 His Asp Val Leu Thr Glu Leu Phe Ser Asn His Phe Ser Thr Leu Val  
 485 490 495  
 Tyr Arg Asn Leu Gln Ile Ala Lys Asn Ser Tyr Asn Asp Ala Leu Leu  
 500 505 510  
 Thr Phe Val Trp Lys Leu Val Ala Asn Phe Arg Arg Gly Phe Arg Lys  
 515 520 525  
 Glu Asp Arg Asn Gly Arg Asp Glu Met Asp Ile Glu Leu His Asp Val  
 530 535 540  
 Ser Pro Ile Thr Arg His Pro Leu Gln Ala Leu Phe Ile Trp Ala Ile  
 545 550 555 560  
 Leu Gln Asn Lys Lys Glu Leu Ser Lys Val Ile Trp Glu Gln Thr Arg  
 565 570 575  
 Gly Cys Thr Leu Ala Ala Leu Gly Ala Ser Lys Leu Leu Lys Thr Leu  
 580 585 590  
 Ala Lys Val Lys Asn Asp Ile Asn Ala Ala Gly Glu Ser Glu Glu Leu  
 595 600 605  
 Ala Asn Glu Tyr Glu Thr Arg Ala Val Glu Leu Phe Thr Glu Cys Tyr  
 610 615 620  
 Ser Ser Asp Glu Asp Leu Ala Glu Gln Leu Leu Val Tyr Ser Cys Glu  
 625 630 635 640  
 Ala Trp Gly Gly Ser Asn Cys Leu Glu Leu Ala Val Glu Ala Thr Asp  
 645 650 655  
 Gln His Phe Thr Ala Gln Pro Gly Val Gln Asn Phe Leu Ser Lys Gln  
 660 665 670

Trp Tyr Gly Glu Ile Ser Arg Asp Thr Lys Asn Trp Lys Ile Ile Leu  
 675 680 685  
 Cys Leu Phe Ile Ile Pro Leu Val Gly Cys Gly Phe Val Ser Phe Arg  
 690 695 700  
 Lys Lys Pro Val Asp Lys His Lys Lys Leu Leu Trp Tyr Tyr Val Ala  
 705 710 715 720  
 Phe Phe Thr Ser Pro Phe Val Val Phe Ser Trp Asn Val Val Phe Tyr  
 725 730 735  
 Ile Ala Phe Leu Leu Leu Phe Ala Tyr Val Leu Leu Met Asp Phe His  
 740 745 750  
 Ser Val Pro His Pro Pro Glu Leu Val Leu Tyr Ser Leu Val Phe Val  
 755 760 765  
 Leu Phe Cys Asp Glu Val Arg Gln Trp Tyr Val Asn Gly Val Asn Tyr  
 770 775 780  
 Phe Thr Asp Leu Trp Asn Val Met Asp Thr Leu Gly Leu Phe Tyr Phe  
 785 790 795 800  
 Ile Ala Gly Ile Val Phe Arg Leu His Ser Ser Asn Lys Ser Ser Leu  
 805 810 815  
 Tyr Ser Gly Arg Val Ile Phe Cys Leu Asp Tyr Ile Ile Phe Thr Leu  
 820 825 830  
 Arg Leu Ile His Ile Phe Thr Val Ser Arg Asn Leu Gly Pro Lys Ile  
 835 840 845  
 Ile Met Leu Gln Arg Met Leu Ile Asp Val Phe Phe Phe Leu Phe Leu  
 850 855 860  
 Phe Ala Val Trp Met Val Ala Phe Gly Val Ala Arg Gln Gly Ile Leu  
 865 870 875 880  
 Arg Gln Asn Glu Gln Arg Trp Arg Trp Ile Phe Arg Ser Val Ile Tyr  
 885 890 895  
 Glu Pro Tyr Leu Ala Met Phe Gly Gln Val Pro Ser Asp Val Asp Gly  
 900 905 910  
 Thr Thr Tyr Asp Phe Ala His Cys Thr Phe Thr Gly Asn Glu Ser Lys  
 915 920 925  
 Pro Leu Cys Val Glu Leu Asp Glu His Asn Leu Pro Arg Phe Pro Glu  
 930 935 940  
 Trp Ile Thr Ile Pro Leu Val Cys Ile Tyr Met Leu Ser Thr Asn Ile  
 945 950 955 960  
 Leu Leu Val Asn Leu Leu Val Ala Met Phe Gly Tyr Thr Val Gly Thr  
 965 970 975  
 Val Gln Glu Asn Asn Asp Gln Val Trp Lys Phe Gln Arg Tyr Phe Leu  
 980 985 990  
 Val Gln Glu Tyr Cys Ser Arg Leu Asn Ile Pro Phe Pro Phe Ile Val  
 995 1000 1005  
 Phe Ala Tyr Phe Tyr Met Val Val Lys Lys Cys Phe Lys Cys Cys Cys  
 1010 1015 1020  
 Lys Glu Lys Asn Met Glu Ser Ser Val Cys Cys Phe Lys Asn Glu Asp  
 1025 1030 1035 1040  
 Asn Glu Thr Leu Ala Trp Glu Gly Val Met Lys Glu Asn Tyr Leu Val  
 1045 1050 1055  
 Lys Ile Asn Thr Lys Ala Asn Asp Thr Ser Glu Glu Met Arg His Arg  
 1060 1065 1070  
 Phe Arg Gln Leu Asp Thr Lys Leu Asn Asp Leu Lys Gly Leu Leu Lys  
 1075 1080 1085  
 Glu Ile Ala Asn Lys Ile Lys  
 1090 1095

&lt;210&gt; 779

&lt;211&gt; 3639

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 779

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gagctcggat ccctagtaac ggccgccagt gtgctggaat tcgcccttgc agccgggctc 120
agcatgagga acagaaggaa tgacactctg gacagcaccg ggacctgtga ctccagcgcg 180
tctcggagca cagacttgtc ttacagtgaag agcgacttgg tgaattttat tcaagcaaat 240
tttaagaaac gagaatgtgt cttctttacc aaagattcca aggccacgga gaatgtgtgc 300
aagtgtggct atgcccagag ccagcacatg gaaggcaccg agatcaacca aagtgagaaa 360
tggaactaca agaaacacac caaggaattt cctaccgacg cctttgggga tattcagttt 420
gagacactgg ggaagaaagg gaagtatata cgtctgtcct gcgacacgga cgcggaaatc 480
ctttacgagc tgctgaccca gcactggcac aatgaaaacac ccaacctggt catttctgtg 540
accgggggcg ccaagaactt cgccctgaag ccgcgcagtc gcaagatctt cagccggctc 600
atctacatcg cgcagtccaa aggtgcttgg attctcacgg gaggcacca ttatggcctg 660
atgaagtaca tcggggaggt ggtgagagat aacaccatca gcaggagtgc agaggagaat 720
attgtggcca ttggcatagc agcttggggc atggtctcca accgggacac cctcatcagg 780
aattgcatg ctgagggcta ttttttagcc cagtacctta tggatgactt cacaagagat 840
ccactgtata tcctggacaa caaccacaca catttctgc tcgtggacaa tggctgtcat 900
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ttcaagtgtt gctgcaagga gaaaaacatg gagtcttctg tctgctgttt caaaaatgaa 3240

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294

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acaaaagcca acgacacctc agaggaaatg aggcacgat ttagacaact ggatacaaag 3360
cttaatgata tcaaggggtct tctgaaagag attgctaata aaatcaaata aaactgtatg 3420
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ttttgctatc gactactaaa tgagagattt tcagaccctt gggtacatgg tggatgattt 3540
taaatacccc tagtgtgctg agaccttgag aataaagtgt gaaggcgaa ttctgcagat 3600
atccatcaca ctggcggcgc ctcgagcatg catctagag 3639

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&lt;210&gt; 780

&lt;211&gt; 1095

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; VARIANT

&lt;222&gt; (1)...(1095)

&lt;223&gt; Xaa = Any Amino Acid

&lt;400&gt; 780

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Met Arg Asn Arg Arg Asn Asp Thr Leu Asp Ser Thr Arg Thr Leu Tyr
              5              10              15
Ser Ser Ala Ser Arg Ser Thr Asp Leu Ser Tyr Ser Glu Ser Asp Leu
              20              25              30
Val Asn Phe Ile Gln Ala Asn Phe Lys Lys Arg Glu Cys Val Phe Phe
              35              40              45
Thr Lys Asp Ser Lys Ala Thr Glu Asn Val Cys Lys Cys Gly Tyr Ala
              50              55              60
Gln Ser Gln His Met Glu Gly Thr Gln Ile Asn Gln Ser Glu Lys Trp
65              70              75              80
Asn Tyr Lys Lys His Thr Lys Glu Phe Pro Thr Asp Ala Phe Gly Asp
              85              90              95
Ile Gln Phe Glu Thr Leu Gly Lys Lys Gly Lys Tyr Ile Arg Leu Ser
              100             105             110
Cys Asp Thr Asp Ala Glu Ile Leu Tyr Glu Leu Leu Thr Gln His Trp
              115             120             125
His Leu Lys Thr Pro Asn Leu Val Ile Ser Val Thr Gly Gly Ala Lys
              130             135             140
Asn Phe Ala Leu Lys Pro Arg Met Arg Lys Ile Phe Ser Arg Leu Ile
145             150             155             160
Tyr Ile Ala Gln Ser Lys Gly Ala Trp Ile Leu Thr Gly Gly Thr His
              165             170             175
Tyr Gly Leu Met Lys Tyr Ile Gly Glu Val Val Arg Asp Asn Thr Ile
              180             185             190
Ser Arg Ser Ser Glu Glu Asn Ile Val Ala Ile Gly Ile Ala Ala Trp
              195             200             205
Gly Met Val Ser Asn Arg Asp Thr Leu Ile Arg Asn Cys Asp Ala Glu
210             215             220
Gly Tyr Phe Leu Ala Gln Tyr Leu Met Asp Asp Phe Thr Arg Asp Pro
225             230             235             240
Leu Tyr Ile Leu Asp Asn Asn His Thr His Leu Leu Leu Val Asp Asn
              245             250             255
Gly Cys His Gly His Pro Thr Val Glu Ala Lys Leu Arg Asn Gln Leu
              260             265             270
Glu Lys Tyr Ile Ser Glu Arg Thr Ile Gln Asp Ser Asn Tyr Gly Gly
              275             280             285
Lys Ile Pro Ile Val Cys Phe Ala Gln Gly Gly Gly Lys Glu Thr Leu
290             295             300
Lys Ala Ile Asn Thr Ser Ile Lys Asn Lys Ile Pro Cys Val Val Val

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295

305					310					315				320	
Glu	Gly	Ser	Gly	Gln	Ile	Ala	Asp	Val	Ile	Ala	Ser	Leu	Val	Glu	Val
				325					330					335	
Glu	Asp	Ala	Leu	Thr	Ser	Ser	Ala	Val	Lys	Glu	Lys	Leu	Val	Arg	Phe
			340						345					350	
Leu	Pro	Arg	Thr	Val	Ser	Arg	Leu	Pro	Glu	Glu	Glu	Thr	Glu	Ser	Trp
		355					360					365			
Ile	Lys	Trp	Leu	Lys	Glu	Ile	Leu	Glu	Cys	Ser	His	Leu	Leu	Thr	Val
	370					375					380				
Ile	Lys	Met	Glu	Glu	Ala	Gly	Asp	Glu	Ile	Val	Ser	Asn	Ala	Ile	Ser
385					390					395					400
Tyr	Ala	Leu	Tyr	Lys	Ala	Phe	Ser	Thr	Ser	Glu	Gln	Asp	Lys	Asp	Asn
				405					410					415	
Trp	Asn	Gly	Gln	Leu	Lys	Leu	Leu	Leu	Glu	Trp	Asn	Gln	Leu	Asp	Leu
		420						425					430		
Ala	Asn	Asp	Glu	Ile	Phe	Thr	Asn	Asp	Arg	Arg	Trp	Glu	Ser	Ala	Asp
	435						440					445			
Leu	Gln	Glu	Val	Met	Phe	Thr	Ala	Leu	Ile	Lys	Asp	Arg	Pro	Lys	Phe
	450						455					460			
Val	Arg	Leu	Phe	Leu	Glu	Asn	Gly	Leu	Asn	Leu	Arg	Lys	Phe	Leu	Thr
465					470					475					480
His	Asp	Val	Leu	Thr	Glu	Leu	Phe	Ser	Asn	His	Phe	Ser	Thr	Leu	Val
				485					490					495	
Tyr	Arg	Asn	Leu	Gln	Ile	Ala	Lys	Asn	Ser	Tyr	Asn	Asp	Ala	Leu	Leu
		500						505					510		
Thr	Phe	Val	Trp	Lys	Leu	Val	Ala	Asn	Phe	Arg	Arg	Gly	Phe	Arg	Lys
	515						520					525			
Glu	Asp	Arg	Asn	Gly	Arg	Asp	Glu	Met	Asp	Ile	Glu	Leu	His	Asp	Val
	530					535					540				
Ser	Pro	Ile	Thr	Arg	His	Pro	Leu	Gln	Ala	Leu	Phe	Ile	Trp	Ala	Ile
545					550					555					560
Leu	Gln	Asn	Lys	Lys	Glu	Leu	Ser	Lys	Val	Ile	Trp	Glu	Gln	Thr	Arg
				565					570					575	
Gly	Cys	Thr	Leu	Ala	Ala	Leu	Gly	Ala	Ser	Lys	Leu	Leu	Lys	Thr	Leu
			580					585					590		
Ala	Lys	Val	Lys	Asn	Asp	Ile	Asn	Ala	Ala	Gly	Glu	Ser	Glu	Glu	Leu
	595						600						605		
Ala	Asn	Glu	Tyr	Glu	Thr	Arg	Ala	Val	Glu	Leu	Phe	Thr	Glu	Cys	Tyr
	610					615						620			
Ser	Ser	Asp	Glu	Asp	Leu	Ala	Glu	Gln	Leu	Leu	Val	Tyr	Ser	Cys	Glu
625					630					635					640
Ala	Trp	Gly	Gly	Ser	Asn	Cys	Leu	Glu	Leu	Ala	Val	Glu	Ala	Thr	Asp
				645					650					655	
Gln	His	Phe	Ile	Ala	Gln	Pro	Gly	Val	Gln	Asn	Phe	Leu	Ser	Lys	Gln
			660					665					670		
Trp	Tyr	Gly	Glu	Ile	Ser	Arg	Asp	Thr	Lys	Asn	Trp	Lys	Ile	Ile	Leu
		675					680					685			
Cys	Leu	Phe	Ile	Ile	Pro	Leu	Val	Gly	Cys	Gly	Phe	Val	Ser	Phe	Arg
	690					695					700				
Lys	Lys	Pro	Val	Asp	Lys	His	Lys	Lys	Leu	Leu	Trp	Tyr	Tyr	Val	Ala
705					710					715					720
Phe	Phe	Thr	Ser	Pro	Phe	Val	Val	Phe	Ser	Trp	Asn	Val	Val	Phe	Tyr
				725					730					735	
Ile	Ala	Phe	Leu	Leu	Phe	Ala	Tyr	Val	Leu	Leu	Met	Asp	Phe	His	
			740					745				750			
Ser	Val	Pro	His	Pro	Pro	Glu	Leu	Val	Leu	Tyr	Ser	Leu	Val	Phe	Val
		755					760					765			
Leu	Phe	Cys	Asp	Glu	Val	Arg	Gln	Trp	Tyr	Val	Asn	Gly	Val	Asn	Tyr



296

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      770      775      780
Phe Thr Asp Leu Trp Asn Val Met Asp Thr Leu Gly Leu Phe Tyr Phe
785      790      795      800
Ile Ala Gly Ile Val Phe Arg Leu His Ser Ser Asn Lys Ser Ser Leu
      805      810      815
Tyr Ser Gly Arg Val Ile Phe Cys Leu Asp Tyr Ile Ile Phe Thr Leu
      820      825      830
Arg Leu Ile His Ile Phe Thr Val Ser Arg Asn Leu Gly Pro Lys Ile
      835      840      845
Ile Met Leu Gln Arg Met Leu Ile Asp Val Phe Phe Phe Leu Phe Leu
      850      855      860
Phe Ala Xaa Trp Met Val Ala Phe Gly Val Ala Arg Gln Gly Ile Leu
865      870      875      880
Arg Gln Asn Glu Gln Arg Trp Arg Trp Ile Phe Arg Ser Val Ile Tyr
      885      890      895
Glu Pro Tyr Leu Ala Met Phe Gly Gln Val Pro Ser Asp Val Asp Gly
      900      905      910
Thr Thr Tyr Asp Phe Ala His Cys Thr Phe Thr Gly Asn Glu Ser Lys
      915      920      925
Pro Leu Cys Val Glu Leu Asp Glu His Asn Leu Pro Arg Phe Pro Glu
      930      935      940
Trp Ile Thr Ile Pro Leu Val Cys Ile Tyr Met Leu Ser Thr Asn Ile
945      950      955      960
Leu Leu Val Asn Leu Leu Val Ala Met Phe Gly Tyr Thr Val Gly Thr
      965      970      975
Val Gln Glu Asn Asn Asp Gln Val Trp Lys Phe Gln Arg Tyr Phe Leu
      980      985      990
Val Gln Glu Tyr Cys Ser Arg Leu Asn Ile Pro Phe Pro Phe Ile Val
      995      1000      1005
Phe Ala Tyr Phe Tyr Met Val Val Lys Lys Cys Phe Lys Cys Cys Cys
      1010      1015      1020
Lys Glu Lys Asn Met Glu Ser Ser Val Cys Cys Phe Lys Asn Glu Asp
1025      1030      1035      1040
Asn Glu Thr Leu Ala Trp Glu Gly Val Met Lys Glu Asn Tyr Leu Val
      1045      1050      1055
Lys Ile Asn Thr Lys Ala Asn Asp Thr Ser Glu Glu Met Arg His Arg
      1060      1065      1070
Phe Arg Gln Leu Asp Thr Lys Leu Asn Asp Leu Lys Gly Leu Leu Lys
      1075      1080      1085
Glu Ile Ala Asn Lys Ile Lys
      1090      1095

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<210> 781  
 <211> 15  
 <212> PRT  
 <213> Homo sapiens

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                   5                  10                  15

<210> 782  
 <211> 45  
 <212> DNA  
 <213> Homo sapiens

<400> 782

297

agaatgccta ccgtgctgca gtgcgtgaac gtgtcgggtgg tgtct 45

<210> 783  
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<212> DNA  
<213> Homo sapiens

<400> 783  
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<210> 784  
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<212> DNA  
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<400> 784  
gagggccgacc aagagccagg gagccagatg gtggaggcca gcctc 45

<210> 785  
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<212> DNA  
<213> Homo sapiens

<400> 785  
ggcctgcaca gtcttgaggc cgaccaagag ccaggagagcc agatg 45

<210> 786  
<211> 45  
<212> DNA  
<213> Homo sapiens

<400> 786  
tacaccatcg ggctgggcct gcacagtctt gagggccgacc aagag 45

<210> 787  
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<212> DNA  
<213> Homo sapiens

<400> 787  
ttccagaact cctacaccat cgggctgggc ctgcacagtc tt 42

<210> 788  
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<400> 788  
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<210> 789  
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<212> DNA  
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<400> 789  
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298

<210> 790  
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<400> 790  
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<210> 791  
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<212> DNA  
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<400> 791  
aacgaattgt tctgctcggg cgtcctggtg catccgcagt ggggtg 45

<210> 792  
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<212> DNA  
<213> Homo sapiens

<400> 792  
gcactggtca tggaaaacga attgttctgc tcgggcgtcc tgggtg 45

<210> 793  
<211> 51  
<212> DNA  
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<400> 793  
tcgcagccct ggcaggcggc actggtcatg gaaaacgaat tgttctgctc g 51

<210> 794  
<211> 45  
<212> DNA  
<213> Homo sapiens

<400> 794  
atcagcattg ctctgcagtg ccctaccgcg gggaactctt gcctc 45

<210> 795  
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<212> DNA  
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<400> 795  
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<210> 796  
<211> 45  
<212> DNA  
<213> Homo sapiens

<400> 796  
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<210> 797

299

<211> 45  
<212> DNA  
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<400> 797  
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<210> 798  
<211> 45  
<212> DNA  
<213> Homo sapiens

<400> 798  
agacccttgc tcgctaacga cctcatgctc atcaagttgg acgaa 45

<210> 799  
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<212> PRT  
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<400> 799  
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5 10 15

<210> 800  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 800  
Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val Glu Ala Ser Leu  
5 10 15

<210> 801  
<211> 15  
<212> PRT  
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<400> 801  
Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met  
5 10 15

<210> 802  
<211> 15  
<212> PRT  
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<400> 802  
Tyr Thr Ile Gly Leu Gly Leu His Ser Leu Glu Ala Asp Gln Glu  
5 10 15

<210> 803  
<211> 14  
<212> PRT

300

&lt;213&gt; Homo sapiens

&lt;400&gt; 803

Phe Gln Asn Ser Tyr Thr Ile Gly Leu Gly Leu His Ser Leu  
5 10

&lt;210&gt; 804

&lt;211&gt; 15

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 804

Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu  
5 10 15

&lt;210&gt; 805

&lt;211&gt; 15

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 805

His Pro Gln Trp Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser  
5 10 15

&lt;210&gt; 806

&lt;211&gt; 15

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 806

Ser Gly Val Leu Val His Pro Gln Trp Val Leu Ser Ala Ala His  
5 10 15

&lt;210&gt; 807

&lt;211&gt; 15

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 807

Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp Val  
5 10 15

&lt;210&gt; 808

&lt;211&gt; 15

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 808

Ala Leu Val Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val  
5 10 15

&lt;210&gt; 809

301

<211> 17  
<212> PRT  
<213> Homo sapiens

<400> 809  
Ser Gln Pro Trp Gln Ala Ala Leu Val Met Glu Asn Glu Leu Phe Cys  
5 10 15

Ser

<210> 810  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 810  
Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly Asn Ser Cys Leu  
5 10 15

<210> 811  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 811  
Ser Val Ser Glu Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser  
5 10 15

<210> 812  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 812  
Ile Lys Leu Asp Glu Ser Val Ser Glu Ser Asp Thr Ile Arg Ser  
5 10 15

<210> 813  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 813  
Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser  
5 10 15

<210> 814  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 814

302

Arg Pro Leu Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu  
                                   5                                  10                                  15

<210> 815  
 <211> 35  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> PCR primer

<400> 815  
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<210> 816  
 <211> 29  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> PCR primer

<400> 816  
 ccgctcgagt ccacccaag cttcacagg 29

<210> 817  
 <211> 1959  
 <212> DNA  
 <213> Homo sapiens

<400> 817  
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 cggagcacag acttgtctta cagtgaagc gacttggtga attttattca agcaaatttt 120  
 aagaaacgag aatgtgtctt ctttacaaa gattccaagg ccacggagaa tgtgtgcaag 180  
 tgtggctatg ccagagcca gcacatggaa ggcaccaga tcaaccaaag tgagaaatgg 240  
 aactacaaga aacacaccaa ggaatttcct accgacgcct ttggggatat tcagtttgag 300  
 acactgggga agaaagggaa gtatatacgt ctgtcctgcg acacggacgc ggaaatcctt 360  
 tacgagctgc tgaccagca ctggcacctg aaaacacca acctgggtcat ttctgtgacc 420  
 gggggcgcca agaacttcgc cctgaagccg cgcattgcga agatcttcag ccggctcatc 480  
 tacatcgcg agtccaaagg tgcttggatt ctacgggag gcaccatta tggcctgatg 540  
 aagtacatcg gggaggtggt gagagataac accatcagca ggagttcaga ggagaatatt 600  
 gtggccattg gcatagcagc ttggggcatg gtctccaacc gggacaccct catcaggaat 660  
 tgcatgctg agggctatct tttagcccag taccttatgg atgacttcac aagagatcca 720  
 ctgtatatcc tggacaacaa ccacacacat ttgtctgctg tggacaatgg ctgtcatgga 780  
 catcccactg tgaagcaaa gctccggaat cagctagaga agtatatctc tgagcgcact 840  
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 aaagagactt tgaagccat caatacctcc atcaaaaata aaattccttg tgtggtggtg 960  
 gaaggctcgg gccagatcgc tgatgtgatc gctagcctgg tggaggtgga ggatgccctg 1020  
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 ctattaacag ttattaaaat ggaagaagct ggggatgaaa ttgtgagcaa tgccatctcc 1200  
 tacgctctat acaaagcctt cagcaccagt gagcaagaca aggataactg gaatgggcag 1260  
 ctgaagcttc tgctggagtg gaaccagctg gacttagcca atgatgagat tttcaccaat 1320  
 gaccgccgat gggagctcgc tgaccttcaa gaagtcattg ttacggctct cataaaggac 1380  
 agaccaagt ttgtccgcct ctttctggag aatggcttga acctacggaa gtttctcacc 1440  
 catgatgtcc tcaactgaact cttctccaac cacttcagca cgcttgtgta ccggaatctg 1500

303

cagatcgcca agaattccta taatgatgcc ctctcacgt ttgtctggaa actggttgcg 1560  
aacttccgaa gaggcttccg gaaggaagac agaaatggcc gggacgagat ggacatagaa 1620  
ctccacgacg tgtctcctat tactcggcac cccctgcaag ctctcttcat ctgggccatt 1680  
cttcagaata agaaggaact ctccaaagtc atttgggagc agaccagggg ctgcactctg 1740  
gcagccctgg gagccagcaa gcttctgaag actctggcca aagtgaagaa cgacatcaat 1800  
gctgctgggg agtccgagga gctggctaag gactacgaga cccgggctgt tgagctgttc 1860  
actgagtgtt acagcagcga tgaagacttg gcagaacagc tgctggtcta ttcctgtgaa 1920  
gcttgggggtg gactcgagca ccaccaccac caccactga 1959

&lt;210&gt; 818

&lt;211&gt; 652

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 818

Met	Arg	Asn	Arg	Arg	Asn	Asp	Thr	Leu	Asp	Ser	Thr	Arg	Thr	Leu	Tyr
				5					10					15	
Ser	Ser	Ala	Ser	Arg	Ser	Thr	Asp	Leu	Ser	Tyr	Ser	Glu	Ser	Asp	Leu
			20					25					30		
Val	Asn	Phe	Ile	Gln	Ala	Asn	Phe	Lys	Lys	Arg	Glu	Cys	Val	Phe	Phe
		35					40					45			
Thr	Lys	Asp	Ser	Lys	Ala	Thr	Glu	Asn	Val	Cys	Lys	Cys	Gly	Tyr	Ala
	50					55					60				
Gln	Ser	Gln	His	Met	Glu	Gly	Thr	Gln	Ile	Asn	Gln	Ser	Glu	Lys	Trp
	65				70					75				80	
Asn	Tyr	Lys	Lys	His	Thr	Lys	Glu	Phe	Pro	Thr	Asp	Ala	Phe	Gly	Asp
				85				90						95	
Ile	Gln	Phe	Glu	Thr	Leu	Gly	Lys	Lys	Gly	Lys	Tyr	Ile	Arg	Leu	Ser
			100					105					110		
Cys	Asp	Thr	Asp	Ala	Glu	Ile	Leu	Tyr	Glu	Leu	Leu	Thr	Gln	His	Trp
		115					120					125			
His	Leu	Lys	Thr	Pro	Asn	Leu	Val	Ile	Ser	Val	Thr	Gly	Gly	Ala	Lys
	130					135					140				
Asn	Phe	Ala	Leu	Lys	Pro	Arg	Met	Arg	Lys	Ile	Phe	Ser	Arg	Leu	Ile
	145				150					155					160
Tyr	Ile	Ala	Gln	Ser	Lys	Gly	Ala	Trp	Ile	Leu	Thr	Gly	Gly	Thr	His
			165					170						175	
Tyr	Gly	Leu	Met	Lys	Tyr	Ile	Gly	Glu	Val	Val	Arg	Asp	Asn	Thr	Ile
		180						185					190		
Ser	Arg	Ser	Ser	Glu	Glu	Asn	Ile	Val	Ala	Ile	Gly	Ile	Ala	Ala	Trp
		195				200						205			
Gly	Met	Val	Ser	Asn	Arg	Asp	Thr	Leu	Ile	Arg	Asn	Cys	Asp	Ala	Glu
	210					215					220				
Gly	Tyr	Phe	Leu	Ala	Gln	Tyr	Leu	Met	Asp	Asp	Phe	Thr	Arg	Asp	Pro
	225				230					235					240
Leu	Tyr	Ile	Leu	Asp	Asn	Asn	His	Thr	His	Leu	Leu	Leu	Val	Asp	Asn
			245						250					255	
Gly	Cys	His	Gly	His	Pro	Thr	Val	Glu	Ala	Lys	Leu	Arg	Asn	Gln	Leu
		260						265					270		
Glu	Lys	Tyr	Ile	Ser	Glu	Arg	Thr	Ile	Gln	Asp	Ser	Asn	Tyr	Gly	Gly
	275						280					285			
Lys	Ile	Pro	Ile	Val	Cys	Phe	Ala	Gln	Gly	Gly	Gly	Lys	Glu	Thr	Leu
	290					295					300				
Lys	Ala	Ile	Asn	Thr	Ser	Ile	Lys	Asn	Lys	Ile	Pro	Cys	Val	Val	Val
	305				310					315					320
Glu	Gly	Ser	Gly	Gln	Ile	Ala	Asp	Val	Ile	Ala	Ser	Leu	Val	Glu	Val
			325					330						335	
Glu	Asp	Ala	Leu	Thr	Ser	Ser	Ala	Val	Lys	Glu	Lys	Leu	Val	Arg	Phe



304

```

      340      345      350
Leu Pro Arg Thr Val Ser Arg Leu Pro Glu Glu Glu Thr Glu Ser Trp
      355      360      365
Ile Lys Trp Leu Lys Glu Ile Leu Glu Cys Ser His Leu Leu Thr Val
      370      375      380
Ile Lys Met Glu Glu Ala Gly Asp Glu Ile Val Ser Asn Ala Ile Ser
385      390      395      400
Tyr Ala Leu Tyr Lys Ala Phe Ser Thr Ser Glu Gln Asp Lys Asp Asn
      405      410      415
Trp Asn Gly Gln Leu Lys Leu Leu Leu Glu Trp Asn Gln Leu Asp Leu
      420      425      430
Ala Asn Asp Glu Ile Phe Thr Asn Asp Arg Arg Trp Glu Ser Ala Asp
      435      440      445
Leu Gln Glu Val Met Phe Thr Ala Leu Ile Lys Asp Arg Pro Lys Phe
      450      455      460
Val Arg Leu Phe Leu Glu Asn Gly Leu Asn Leu Arg Lys Phe Leu Thr
465      470      475      480
His Asp Val Leu Thr Glu Leu Phe Ser Asn His Phe Ser Thr Leu Val
      485      490      495
Tyr Arg Asn Leu Gln Ile Ala Lys Asn Ser Tyr Asn Asp Ala Leu Leu
      500      505      510
Thr Phe Val Trp Lys Leu Val Ala Asn Phe Arg Arg Gly Phe Arg Lys
      515      520      525
Glu Asp Arg Asn Gly Arg Asp Glu Met Asp Ile Glu Leu His Asp Val
      530      535      540
Ser Pro Ile Thr Arg His Pro Leu Gln Ala Leu Phe Ile Trp Ala Ile
545      550      555      560
Leu Gln Asn Lys Lys Glu Leu Ser Lys Val Ile Trp Glu Gln Thr Arg
      565      570      575
Gly Cys Thr Leu Ala Ala Leu Gly Ala Ser Lys Leu Leu Lys Thr Leu
      580      585      590
Ala Lys Val Lys Asn Asp Ile Asn Ala Ala Gly Glu Ser Glu Glu Leu
      595      600      605
Ala Asn Glu Tyr Glu Thr Arg Ala Val Glu Leu Phe Thr Glu Cys Tyr
      610      615      620
Ser Ser Asp Glu Asp Leu Ala Glu Gln Leu Leu Val Tyr Ser Cys Glu
625      630      635      640
Ala Trp Gly Gly Leu Glu His His His His His His
      645      650

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&lt;210&gt; 819

&lt;211&gt; 132

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 819

```

Thr Ala Ala Ser Asp Asn Phe Gln Leu Ser Gln Gly Gly Gln Gly Phe
1      5      10      15
Ala Ile Pro Ile Gly Gln Ala Met Ala Ile Ala Gly Gln Ile Arg Ser
      20      25      30
Gly Gly Gly Ser Pro Thr Val His Ile Gly Pro Thr Ala Phe Leu Gly
      35      40      45
Leu Gly Val Val Asp Asn Asn Gly Asn Gly Ala Arg Val Gln Arg Val
      50      55      60
Val Gly Ser Ala Pro Ala Ala Ser Leu Gly Ile Ser Thr Gly Asp Val
65      70      75      80
Ile Thr Ala Val Asp Gly Ala Pro Ile Asn Ser Ala Thr Ala Met Ala

```

305

			85					90				95			
Asp	Ala	Leu	Asn	Gly	His	His	Pro	Gly	Asp	Val	Ile	Ser	Val	Asn	Trp
			100					105					110		
Gln	Thr	Lys	Ser	Gly	Gly	Thr	Arg	Thr	Gly	Asn	Val	Thr	Leu	Ala	Glu
			115				120					125			
Gly	Pro	Pro	Ala												
			130												

<210> 820  
 <211> 36  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> PCR primer

<400> 820  
 gggaattca tgatccggga gaaatttgcc cactgc 36

<210> 821  
 <211> 33  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> PCR primer

<400> 821  
 gggtcagat caggagtttg agaccagcct ggc 33

<210> 822  
 <211> 675  
 <212> DNA  
 <213> Homo sapiens

<400> 822  
 atgcatcacc atcaccatca cacggccgcg tccgataact tccagctgtc ccaggggtggg 60  
 cagggattcg ccattccgat cgggcaggcg atggcgatcg cgggccagat caagcttccc 120  
 accgttcata tggggcctac cgccttcctc ggcttgggtg ttgtcgacaa caacggcaac 180  
 ggcgcacgag tccaacgcgt ggtcgggagc gctccggcgg caagtctcgg catctccacc 240  
 ggcgacgtga tcaccgcggt cgacggcgct ccgatcaact cggccaccgc gatggcggac 300  
 gcgcttaacg ggcacatcc cggtgacgtc atctcgggtga cctggcaaac caagtcgggc 360  
 ggcacgcgta cagggaacgt gacattggcc gagggacccc cggccgaatt catgatccgg 420  
 gagaaatttg ccactgcac cgtgctaacc attgcacaca gattgaacac cattattgac 480  
 agcgacaaga taatggtttt agattcagga agactgaaag aatatgatga gccgtatgtt 540  
 ttgctgcaaa ataaagagag cctatttttac aagatggtgc aacaactggg caaggcagaa 600  
 gccgctgccc tactgaaac agcaaaacag agatggggtt tcaccatgtt ggccaggctg 660  
 gtctcaaact cctga 675

<210> 823  
 <211> 291  
 <212> DNA  
 <213> Homo sapiens

306

&lt;400&gt; 823

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atgggggatcc gggagaaatt tgcccactgc accgtgctaa ccattgcaca cagattgaac 60
accattatttg acagcgacaa gataatgggt ttagattcag gaagactgaa agaataatgat 120
gagccgtatg ttttgctgca aaataaagag agcctatattt acaagatggg gcaacaactg 180
ggcaaggcag aagccgctgc cctcaactgaa acagcaaaac agagatgggg tttcaccatg 240
ttggccaggc tgggtctcaa ctccctcgag caccaccacc accaccactg a 291

```

&lt;210&gt; 824

&lt;211&gt; 1074

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 824

```

atgtcagcca ttgagagggt gtcagaggca atcgtcagca tccgaagaat ccagaccttt 60
ttgctacttg atgagatatc acagcgcaac cgtcagctgc cgtcagatgg taaaaagatg 120
gtgcatgtgc aggattttac tgcttttttg gataaggcat cagagacccc aactctacaa 180
ggccttttct tttactgtcag acctggcgaa ttgttagctg tggtcggccc cgtgggagca 240
gggaagtcac cactgttaag tgccgtgctc ggggaattgg cccaagtca cgggctggtc 300
agcgtgcatg gaagaattgc ctatgtgtct cagcagccct ggggtgttctc gggaactctg 360
aggagtaata ttttattttg gaagaaatac gaaaaggaaac gatatgaaaa agtcataaag 420
gcttgtgctc tgaaaaagga tttacagctg ttggaggatg gtgatctgac tgtgatagga 480
gatcggggaa ccacgctgag tggagggcag aaagcacggg taaaccttgc aagagcagtg 540
tatcaagatg ctgacatcta tctcctggac gatcctctca gtgcagtaga tgcggaagtt 600
agcagacact tgttcgaact gtgtattttg caaattttgc atgagaagat cacaatttta 660
gtgactcatc agttgcagta cctcaaagct gcaagtcaga ttctgatatt gaaagatggg 720
aaaatggtgc agaaggggac ttacactgag ttccctaaaat ctggatataga ttttggctcc 780
cttttaaaaga aggataatga ggaaagtga caacctccag ttccaggaac tcccacacta 840
aggaatcgta ccttctcaga gtcttcggtt tgggtctcaac aatcttctag accctccttg 900
aaagatgggt ctctggagag ccaagataca gagaatgtcc cagttacact atcagaggag 960
aaccgttctg aaggaaaagt tggttttcag gcctataaga attacttcag agctgggtgct 1020
cactggattg tcttcatttt ccttattctc gagcaccacc accaccacca ctga 1074

```

&lt;210&gt; 825

&lt;211&gt; 224

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 825

```

Met His His His His His Thr Ala Ala Ser Asp Asn Phe Gln Leu
                    5                10                15
Ser Gln Gly Gly Gln Gly Phe Ala Ile Pro Ile Gly Gln Ala Met Ala
                    20                25                30
Ile Ala Gly Gln Ile Lys Leu Pro Thr Val His Ile Gly Pro Thr Ala
                    35                40                45
Phe Leu Gly Leu Gly Val Val Asp Asn Asn Gly Asn Gly Ala Arg Val
                    50                55                60
Gln Arg Val Val Gly Ser Ala Pro Ala Ala Ser Leu Gly Ile Ser Thr
                    65                70                75                80
Gly Asp Val Ile Thr Ala Val Asp Gly Ala Pro Ile Asn Ser Ala Thr
                    85                90                95
Ala Met Ala Asp Ala Leu Asn Gly His His Pro Gly Asp Val Ile Ser
                    100               105               110
Val Thr Trp Gln Thr Lys Ser Gly Gly Thr Arg Thr Gly Asn Val Thr
                    115               120               125
Leu Ala Glu Gly Pro Pro Ala Glu Phe Met Ile Arg Glu Lys Phe Ala
                    130               135               140
His Cys Thr Val Leu Thr Ile Ala His Arg Leu Asn Thr Ile Ile Asp

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307

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145          150          155          160
Ser Asp Lys Ile Met Val Leu Asp Ser Gly Arg Leu Lys Glu Tyr Asp
          165          170          175
Glu Pro Tyr Val Leu Leu Gln Asn Lys Glu Ser Leu Phe Tyr Lys Met
          180          185          190
Val Gln Gln Leu Gly Lys Ala Glu Ala Ala Ala Leu Thr Glu Thr Ala
          195          200          205
Lys Gln Arg Trp Gly Phe Thr Met Leu Ala Arg Leu Val Ser Asn Ser
          210          215          220

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&lt;210&gt; 826

&lt;211&gt; 357

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 826

```

Met Ser Ala Ile Glu Arg Val Ser Glu Ala Ile Val Ser Ile Arg Arg
          5          10          15
Ile Gln Thr Phe Leu Leu Leu Asp Glu Ile Ser Gln Arg Asn Arg Gln
          20          25          30
Leu Pro Ser Asp Gly Lys Lys Met Val His Val Gln Asp Phe Thr Ala
          35          40          45
Phe Trp Asp Lys Ala Ser Glu Thr Pro Thr Leu Gln Gly Leu Ser Phe
          50          55          60
Thr Val Arg Pro Gly Glu Leu Leu Ala Val Val Gly Pro Val Gly Ala
          65          70          75          80
Gly Lys Ser Ser Leu Leu Ser Ala Val Leu Gly Glu Leu Ala Pro Ser
          85          90          95
His Gly Leu Val Ser Val His Gly Arg Ile Ala Tyr Val Ser Gln Gln
          100          105          110
Pro Trp Val Phe Ser Gly Thr Leu Arg Ser Asn Ile Leu Phe Gly Lys
          115          120          125
Lys Tyr Glu Lys Glu Arg Tyr Glu Lys Val Ile Lys Ala Cys Ala Leu
          130          135          140
Lys Lys Asp Leu Gln Leu Leu Glu Asp Gly Asp Leu Thr Val Ile Gly
145          150          155          160
Asp Arg Gly Thr Thr Leu Ser Gly Gly Gln Lys Ala Arg Val Asn Leu
          165          170          175
Ala Arg Ala Val Tyr Gln Asp Ala Asp Ile Tyr Leu Leu Asp Asp Pro
          180          185          190
Leu Ser Ala Val Asp Ala Glu Val Ser Arg His Leu Phe Glu Leu Cys
          195          200          205
Ile Cys Gln Ile Leu His Glu Lys Ile Thr Ile Leu Val Thr His Gln
          210          215          220
Leu Gln Tyr Leu Lys Ala Ala Ser Gln Ile Leu Ile Leu Lys Asp Gly
225          230          235          240
Lys Met Val Gln Lys Gly Thr Tyr Thr Glu Phe Leu Lys Ser Gly Ile
          245          250          255
Asp Phe Gly Ser Leu Leu Lys Lys Asp Asn Glu Glu Ser Glu Gln Pro
          260          265          270
Pro Val Pro Gly Thr Pro Thr Leu Arg Asn Arg Thr Phe Ser Glu Ser
          275          280          285
Ser Val Trp Ser Gln Gln Ser Ser Arg Pro Ser Leu Lys Asp Gly Ala
          290          295          300
Leu Glu Ser Gln Asp Thr Glu Asn Val Pro Val Thr Leu Ser Glu Glu
305          310          315          320
Asn Arg Ser Glu Gly Lys Val Gly Phe Gln Ala Tyr Lys Asn Tyr Phe

```

308

325 330 335  
 Arg Ala Gly Ala His Trp Ile Val Phe Ile Phe Leu Ile Leu Glu His  
 340 345 350  
 His His His His His  
 355

<210> 827  
 <211> 96  
 <212> PRT  
 <213> Homo sapiens

<400> 827  
 Met Gly Ile Arg Glu Lys Phe Ala His Cys Thr Val Leu Thr Ile Ala  
 5 10 15  
 His Arg Leu Asn Thr Ile Ile Asp Ser Asp Lys Ile Met Val Leu Asp  
 20 25 30  
 Ser Gly Arg Leu Lys Glu Tyr Asp Glu Pro Tyr Val Leu Leu Gln Asn  
 35 40 45  
 Lys Glu Ser Leu Phe Tyr Lys Met Val Gln Gln Leu Gly Lys Ala Glu  
 50 55 60  
 Ala Ala Ala Leu Thr Glu Thr Ala Lys Gln Arg Trp Gly Phe Thr Met  
 65 70 75 80  
 Leu Ala Arg Leu Val Ser Asn Ser Leu Glu His His His His His His  
 85 90 95

<210> 828  
 <211> 35  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> PCR primer

<400> 828  
 cgcccatggg gatccgggag aaatttgccc actgc 35

<210> 829  
 <211> 35  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> PCR primer

<400> 829  
 cgcctcgagg gagtttgaga ccagcctggc caaca 35

<210> 830  
 <211> 38  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> PCR primer

<400> 830

309

gcatggacca tatgtcagcc attgagaggg tgtcagag 38

<210> 831  
 <211> 34  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> PCR primer

<400> 831  
 ccgctcgaga ataaggaaaa tgaagacaat ccag 34

<210> 832  
 <211> 27  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> PCR primer

<400> 832  
 gttgaattca tgcacgggcc ccaggtg 27

<210> 833  
 <211> 30  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> PCR primer

<400> 833  
 cccctcgagt cactatgggtc tgcctcttga 30

<210> 834  
 <211> 915  
 <212> DNA  
 <213> Homo sapiens

<400> 834  
 atgcatcacc atcaccatca cacggccgag tccgataact tccagctgtc ccagggtggg 60  
 cagggtattcg ccattccgat cgggcaggcg atggcgatcg cgggccagat caagcttccc 120  
 accgttcata tcgggcctac cgccttctc ggcttgggtg ttgtcgacaa caacggcaac 180  
 ggcgcacgag tccaacgcgt ggtcgggagc gctccggcgg caagtctcgg catctccacc 240  
 ggcgacgtga tcaccgcgtg cgacggcgct ccgatcaact cggccaccgc gatggcggac 300  
 gcgcttaacg ggcacatcc cggtgacgtc atctcggtga cctggcaaac caagtcgggc 360  
 ggacgcgta cagggaacgt gacattggcc gagggacccc cggccgaatt catgcacggg 420  
 cccaggtgc tggcacgctg ctccgagtg gcttgcctg ccttggctgc cacctctgcg 480  
 ggggtgcgtc tggagggggg ggaccggcca ccaaccttac ccagtcaagg aagtggatgg 540  
 ccatgttccc acagcctgag tggctgccac ctgatggctg atggagcaaa ggccttagga 600  
 aaagcagatg gcccttggcc ctaccttttt gttagaagaa ctgatgttcc atgtcctgca 660  
 gcgagtgagg ttggtggctg tgccccagc tcctggcgcg ccctcgaga ggtgactggg 720  
 tgctcttttg gccctcttgg ccttgcccag catgcacaag cctcagtgt actactgtgc 780

310

tacaaatgga gccatatagg ggaaacgagc agccatctca ggagcaaggt gtatgctgcc 840  
 ttgggggct ccagtccttg cctcaagggt cttatgtcac tgtgggcttc ttgggtgtca 900  
 agaggcagac catag 915

<210> 835  
 <211> 304  
 <212> PRT  
 <213> Homo sapiens

<400> 835  
 Met His His His His His Thr Ala Ala Ser Asp Asn Phe Gln Leu  
                   5                  10                  15  
 Ser Gln Gly Gly Gln Gly Phe Ala Ile Pro Ile Gly Gln Ala Met Ala  
                   20                  25                  30  
 Ile Ala Gly Gln Ile Lys Leu Pro Thr Val His Ile Gly Pro Thr Ala  
                   35                  40                  45  
 Phe Leu Gly Leu Gly Val Val Asp Asn Asn Gly Asn Gly Ala Arg Val  
                   50                  55                  60  
 Gln Arg Val Val Gly Ser Ala Pro Ala Ala Ser Leu Gly Ile Ser Thr  
                   65                  70                  75                  80  
 Gly Asp Val Ile Thr Ala Val Asp Gly Ala Pro Ile Asn Ser Ala Thr  
                   85                  90                  95  
 Ala Met Ala Asp Ala Leu Asn Gly His His Pro Gly Asp Val Ile Ser  
                   100                  105                  110  
 Val Thr Trp Gln Thr Lys Ser Gly Gly Thr Arg Thr Gly Asn Val Thr  
                   115                  120                  125  
 Leu Ala Glu Gly Pro Pro Ala Glu Phe Met His Gly Pro Gln Val Leu  
                   130                  135                  140  
 Ala Arg Cys Ser Glu Cys Ala Cys Pro Ala Leu Ala Ala Thr Ser Ala  
                   145                  150                  155                  160  
 Gly Val Arg Leu Glu Gly Val Asp Arg Pro Pro Thr Leu Pro Ser Gln  
                   165                  170                  175  
 Gly Ser Gly Trp Pro Cys Ser His Ser Leu Ser Gly Cys His Leu Met  
                   180                  185                  190  
 Ala Asp Gly Ala Lys Ala Leu Gly Lys Ala Asp Gly Pro Trp Pro Tyr  
                   195                  200                  205  
 Leu Phe Val Arg Arg Thr Asp Val Pro Cys Pro Ala Ala Ser Glu Val  
                   210                  215                  220  
 Gly Gly Cys Ala Pro Ser Ser Trp Arg Ala Leu Ala Glu Val Thr Gly  
                   225                  230                  235                  240  
 Cys Ser Leu Gly Pro Leu Gly Leu Ala Gln His Ala Gln Ala Ser Val  
                   245                  250                  255  
 Leu Leu Leu Cys Tyr Lys Trp Ser His Ile Gly Glu Thr Ser Ser His  
                   260                  265                  270  
 Leu Arg Ser Lys Val Tyr Ala Ala Phe Gly Gly Ser Ser Pro Cys Leu  
                   275                  280                  285  
 Lys Gly Leu Met Ser Leu Trp Ala Ser Trp Leu Ser Arg Gly Arg Pro  
                   290                  295                  300

<210> 836  
 <211> 24  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> PCR primer

<400> 836

311

cgaagtcacg tggaggccag cctc

24

&lt;210&gt; 837

&lt;211&gt; 29

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; PCR primer

&lt;400&gt; 837

cctgaccgaa ttcattaact ggcctggac

29

&lt;210&gt; 838

&lt;211&gt; 166

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; VARIANT

&lt;222&gt; (1)...(166)

&lt;223&gt; Xaa = Any Amino Acid

&lt;400&gt; 838

Met	Gly	His	His	His	His	His	His	Val	Glu	Ala	Ser	Leu	Ser	Val	Arg
1				5					10					15	
His	Pro	Glu	Tyr	Asn	Arg	Pro	Leu	Leu	Ala	Asn	Asp	Leu	Met	Leu	Ile
		20					25					30			
Lys	Leu	Asp	Glu	Ser	Val	Ser	Glu	Ser	Asp	Thr	Ile	Arg	Ser	Ile	Ser
		35					40					45			
Ile	Ala	Ser	Gln	Cys	Pro	Thr	Ala	Gly	Asn	Ser	Cys	Leu	Val	Ser	Gly
	50					55					60				
Trp	Gly	Leu	Leu	Ala	Asn	Gly	Arg	Met	Pro	Thr	Val	Leu	Gln	Cys	Val
65					70					75					80
Asn	Val	Ser	Val	Val	Ser	Glu	Glu	Val	Cys	Ser	Lys	Leu	Tyr	Asp	Pro
				85					90					95	
Leu	Tyr	His	Pro	Ser	Met	Phe	Cys	Ala	Gly	Gly	Gly	Gln	Xaa	Gln	Xaa
			100					105					110		
Asp	Ser	Cys	Asn	Gly	Asp	Ser	Gly	Gly	Pro	Leu	Ile	Cys	Asn	Gly	Tyr
		115					120					125			
Leu	Gln	Gly	Leu	Val	Ser	Phe	Gly	Lys	Ala	Pro	Cys	Gly	Gln	Val	Gly
	130					135					140				
Val	Pro	Gly	Val	Tyr	Thr	Asn	Leu	Cys	Lys	Phe	Thr	Glu	Trp	Ile	Glu
145					150					155					160
Lys	Thr	Val	Gln	Ala	Ser										
					165										

&lt;210&gt; 839

&lt;211&gt; 504

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(504)

&lt;223&gt; n = A,T,C or G



312

<400> 839  
 atggggccatc atcatcatca tcacgtggag gccagcctct ccgtacggca cccagagtac 60  
 aacagaccct tgctcgctaa cgacctcatg ctcatcaagt tggacgaatc cgtgtccgag 120  
 tctgacacca tccggagcat cagcattgct tcgcagtgcc ctaccgcggg gaactcttgc 180  
 ctcgtttctg gctgggtct gctggcgaac ggcagaatgc ctaccgtgct gcagtgcgtg 240  
 aacgtgtcgg tgggtgtctga ggaggtctgc agtaagctct atgaccgcgt gtaccacccc 300  
 agcatgttct gcgcggcgagg agggcaanac cagaangact cctgcaacgg tgactctggg 360  
 gggcccctga tctgcaacgg gtacttgacg ggccttgtgt ctttcggaaa agccccgtgt 420  
 ggccaagtgt gcgtgccagg tgtctacacc aacctctgca aattcactga gtggatagag 480  
 aaaaccgtcc aggccagtta atga 504

<210> 840  
 <211> 21  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> PCR primer

<400> 840  
 ctcagggttc cggagccgcg g 21

<210> 841  
 <211> 35  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> PCR primer

<400> 841  
 ctatagaatt cattaccaa aagctgggct ccagc 35

<210> 842  
 <211> 241  
 <212> PRT  
 <213> Homo sapiens

<400> 842  
 Met Gln His His His His His His Leu Arg Val Pro Glu Pro Arg Pro  
 1 5 10 15  
 Gly Glu Ala Lys Ala Glu Gly Ala Ala Pro Pro Thr Pro Ser Lys Pro  
 20 25 30  
 Leu Thr Ser Phe Leu Ile Gln Asp Ile Leu Arg Asp Gly Ala Gln Arg  
 35 40 45  
 Gln Gly Gly Arg Thr Ser Ser Gln Arg Gln Arg Asp Pro Glu Pro Glu  
 50 55 60  
 Pro Glu Pro Glu Pro Glu Gly Gly Arg Ser Arg Ala Gly Ala Gln Asn  
 65 70 75 80  
 Asp Gln Leu Ser Thr Gly Pro Arg Ala Ala Pro Glu Glu Ala Glu Thr  
 85 90 95  
 Leu Ala Glu Thr Glu Pro Glu Arg His Leu Gly Ser Tyr Leu Leu Asp  
 100 105 110  
 Ser Glu Asn Thr Ser Gly Ala Leu Pro Arg Leu Pro Gln Thr Pro Lys  
 115 120 125

313

Gln Pro Gln Lys Arg Ser Arg Ala Ala Phe Ser His Thr Gln Val Ile  
 130 135 140  
 Glu Leu Glu Arg Lys Phe Ser His Gln Lys Tyr Leu Ser Ala Pro Glu  
 145 150 155 160  
 Arg Ala His Leu Ala Lys Asn Leu Lys Leu Thr Glu Thr Gln Val Lys  
 165 170 175  
 Ile Trp Phe Gln Asn Arg Arg Tyr Lys Thr Lys Arg Lys Gln Leu Ser  
 180 185 190  
 Ser Glu Leu Gly Asp Leu Glu Lys His Ser Ser Leu Pro Ala Leu Lys  
 195 200 205  
 Glu Glu Ala Phe Ser Arg Ala Ser Leu Val Ser Val Tyr Asn Ser Tyr  
 210 215 220  
 Pro Tyr Tyr Pro Tyr Leu Tyr Cys Val Gly Ser Trp Ser Pro Ala Phe  
 225 230 235 240  
 Trp

<210> 843  
 <211> 729  
 <212> DNA  
 <213> Homo sapiens

<400> 843  
 atgcagcatc accaccatca ccacctcagg gttccggagc cgcggcccgg ggaggcgaaa 60  
 gcggaggggg ccgcgcgcgc gaccccgctc aagccgctca cgtccttcct catccaggac 120  
 atcctgcggg acggcgcgca gcggcaaggc ggccgcacga gcagccagag acagcgcgac 180  
 ccggagccgg agccagagcc agagccagag ggaggacgca gccgcgccgg ggcgcagaac 240  
 gaccagctga gcaccggggcc ccgcgcgcgc ccggatgagg ccgagacgct ggagagacc 300  
 gagccagaaa ggcacttggg gtcttatctg ttggactctg aaaacacttc aggcgcctt 360  
 ccaaggcttc cccaaacccc taagcagccg cagaagcgt cccgagctgc cttctccac 420  
 actcaggtga tgcagttgga gaggaagttc agccatcaga agtacctgtc ggcccctgaa 480  
 cgggccacc tggccaagaa cctcaagctc acggagaccc aagtgaagat atggttccag 540  
 aacagacgct ataagactaa gcgaaagcag ctctcctcgg agctgggaga cttggagaag 600  
 cactcctttt tgccggccct gaaagaggag gccttctccc gggcctccct ggtctccgtg 660  
 tataacagct atccttacta ccatacctg cactgcgtgg gcagctggag ccagctttt 720  
 tggtaatga 729

<210> 844  
 <211> 27  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> PCR primer

<400> 844  
 ctactaagcg ctggagtgg ggatcag

27

<210> 845  
 <211> 33  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> PCR primer

314

<400> 845  
catcgagaat tcactactct ctgactagat gtc

33

<210> 846  
<211> 161  
<212> PRT  
<213> Homo sapiens

<400> 846  
Met Gln His His His His His His Ala Gly Val Arg Asp Gln Gly Gln  
1 5 10 15  
Gly Ala Arg Trp Pro His Thr Gly Lys Arg Gly Pro Leu Leu Gln Gly  
20 25 30  
Leu Thr Trp Ala Thr Gly Gly His Cys Phe Ser Ser Glu Glu Ser Gly  
35 40 45  
Ala Val Asp Gly Ala Gly Gln Lys Lys Asp Arg Ala Trp Leu Arg Cys  
50 55 60  
Pro Glu Ala Val Ala Gly Phe Pro Leu Gly Ser Asp Cys Arg Glu Gly  
65 70 75 80  
Gly Arg Gln Gly Cys Gly Gly Ser Asp Asp Glu Asp Asp Leu Gly Val  
85 90 95  
Ala Pro Gly Leu Ala Pro Ala Trp Ala Leu Thr Gln Pro Pro Ser Gln  
100 105 110  
Ser Pro Gly Pro Gln Ser Leu Pro Ser Thr Pro Ser Ser Ile Trp Pro  
115 120 125  
Gln Trp Val Ile Leu Ile Thr Glu Leu Thr Ile Pro Ser Pro Ala His  
130 135 140  
Gly Pro Pro Trp Leu Pro Asn Ala Leu Glu Arg Gly His Leu Val Arg  
145 150 155 160  
Glu

<210> 847  
<211> 489  
<212> DNA  
<213> Homo sapiens

<400> 847  
atgcagcatc accaccatca ccacgctgga gtgagggatc aggggcaggg cgcgagatgg 60  
cctcacacag ggaagagagg gccctcctg cagggcctca cctgggccac aggaggacac 120  
tgcttttcct ctgaggagtc aggagctgtg gatggtgctg gacagaagaa ggacagggcc 180  
tggctcaggt gtccagaggc tgctgctggc ttccctttgg gatcagactg cagggaggga 240  
gggcggcagg gttgtggggg gagtgacgat gaggatgacc tgggggtggc tccaggcctt 300  
gccctgcct gggccctcac ccagcctccc tcacagtctc ctggccctca gtctctcccc 360  
tccactccat cctccatctg gcctcagtgg gtcattctga tctactgaact gaccataccc 420  
agccctgccc acggccctcc atggctcccc aatgccctgg agaggggaca tctagtcaga 480  
gagtagtga 489

<210> 848  
<211> 132  
<212> PRT  
<213> Homo sapiens

<400> 848  
Thr Ala Ala Ser Asp Asn Phe Gln Leu Ser Gln Gly Gly Gln Gly Phe

315

```

1           5           10           15
Ala Ile Pro Ile Gly Gln Ala Met Ala Ile Ala Gly Gln Ile Arg Ser
                20           25           30
Gly Gly Gly Ser Pro Thr Val His Ile Gly Pro Thr Ala Phe Leu Gly
                35           40           45
Leu Gly Val Val Asp Asn Asn Gly Asn Gly Ala Arg Val Gln Arg Val
                50           55           60
Val Gly Ser Ala Pro Ala Ala Ser Leu Gly Ile Ser Thr Gly Asp Val
                65           70           75           80
Ile Thr Ala Val Asp Gly Ala Pro Ile Asn Ser Ala Thr Ala Met Ala
                85           90           95
Asp Ala Leu Asn Gly His His Pro Gly Asp Val Ile Ser Val Asn Trp
                100           105           110
Gln Thr Lys Ser Gly Gly Thr Arg Thr Gly Asn Val Thr Leu Ala Glu
                115           120           125
Gly Pro Pro Ala
                130

```

<210> 849  
 <211> 31  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> PCR primer

<400> 849  
 ggggaattca tcacctatgt gccgcctctg c

31

<210> 850  
 <211> 40  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> PCR primer

<400> 850  
 gggctcgagt cactcgccca cgaaatccgt gtaaaacagc

40

<210> 851  
 <211> 1203  
 <212> DNA  
 <213> Homo sapiens

<400> 851  
 atgcatcacc atcaccatca cacggccgog tccgataact tccagctgtc ccagggtggg 60  
 cagggtattcg ccattccgat cgggcaggcg atggcgatcg cgggccagat caagcttccc 120  
 accgttcata tcgggcctac cgccttcctc ggcttgggtg ttgtcgacaa caacggcaac 180  
 ggcgcacgag tccaacgcgt ggtcgggagc gctccggcgg caagtctcgg catctccacc 240  
 ggcgacgtga tcaccgcggt cgacggcgct ccgatcaact cggccaccgc gatggcggac 300  
 gcgcttaacg ggcacatcc cggtagcgct atctcggtga cctggcaaac caagtcgggc 360  
 ggcacgcgta cagggaacgt gacattggcc gagggacccc cggccgaatt catcacctat 420  
 gtgccgcctc tgctgctgga agtgggggta gaggagaagt tcatgaccat ggtgctgggc 480  
 attggtccag tgctgggcct ggtctgtgtc ccgctcctag gctcagccag tgaccactgg 540  
 cgtggacgct atggccgccc cgggcccttc atctgggcac tgtccttggg catcctgctg 600

316

```

agcctctttc tcatcccaag ggccggctgg ctagcagggc tgctgtgccc ggatcccagg 660
cccctggagc tggcactgct catcctgggc gtggggctgc tggacttctg tggccagggtg 720
tgcttcactc cactggaggc cctgctctct gacctcttcc gggacccgga ccactgtcgc 780
caggcctact ctgtctatgc cttcatgac agtcttgggg gctgcctggg ctacctcctg 840
cctgccattg actgggacac cagtgcctg gcccctacc tgggcaccca ggaggagtgc 900
ctctttggcc tgctcaccct catcttcctc acctgcgtag cagccacact gctgggtggct 960
gaggaggcag cgctgggccc caccgagcca gcagaagggc tgtcggcccc ctccttgtcg 1020
ccccactgct gtccatgccg ggcccgttg gctttccgga acctgggcgc cctgcttccc 1080
cggctgcacc agctgtgctg ccgcatgccc cgcaccctgc gccggctctt cgtggctgag 1140
ctgtgcagct ggatggcact catgaccttc acgctgtttt acacggattt cgtgggcgag 1200
tga 1203

```

&lt;210&gt; 852

&lt;211&gt; 400

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 852

```

Met His His His His His Thr Ala Ala Ser Asp Asn Phe Gln Leu
      5              10              15
Ser Gln Gly Gly Gln Gly Phe Ala Ile Pro Ile Gly Gln Ala Met Ala
      20              25              30
Ile Ala Gly Gln Ile Lys Leu Pro Thr Val His Ile Gly Pro Thr Ala
      35              40              45
Phe Leu Gly Leu Gly Val Val Asp Asn Asn Gly Asn Gly Ala Arg Val
      50              55              60
Gln Arg Val Val Gly Ser Ala Pro Ala Ala Ser Leu Gly Ile Ser Thr
      65              70              75              80
Gly Asp Val Ile Thr Ala Val Asp Gly Ala Pro Ile Asn Ser Ala Thr
      85              90              95
Ala Met Ala Asp Ala Leu Asn Gly His His Pro Gly Asp Val Ile Ser
      100             105             110
Val Thr Trp Gln Thr Lys Ser Gly Gly Thr Arg Thr Gly Asn Val Thr
      115             120             125
Leu Ala Glu Gly Pro Pro Ala Glu Phe Ile Thr Tyr Val Pro Pro Leu
      130             135             140
Leu Leu Glu Val Gly Val Glu Glu Lys Phe Met Thr Met Val Leu Gly
      145             150             155             160
Ile Gly Pro Val Leu Gly Leu Val Cys Val Pro Leu Leu Gly Ser Ala
      165             170             175
Ser Asp His Trp Arg Gly Arg Tyr Gly Arg Arg Arg Pro Phe Ile Trp
      180             185             190
Ala Leu Ser Leu Gly Ile Leu Leu Ser Leu Phe Leu Ile Pro Arg Ala
      195             200             205
Gly Trp Leu Ala Gly Leu Leu Cys Pro Asp Pro Arg Pro Leu Glu Leu
      210             215             220
Ala Leu Leu Ile Leu Gly Val Gly Leu Leu Asp Phe Cys Gly Gln Val
      225             230             235             240
Cys Phe Thr Pro Leu Glu Ala Leu Leu Ser Asp Leu Phe Arg Asp Pro
      245             250             255
Asp His Cys Arg Gln Ala Tyr Ser Val Tyr Ala Phe Met Ile Ser Leu
      260             265             270
Gly Gly Cys Leu Gly Tyr Leu Leu Pro Ala Ile Asp Trp Asp Thr Ser
      275             280             285
Ala Leu Ala Pro Tyr Leu Gly Thr Gln Glu Glu Cys Leu Phe Gly Leu
      290             295             300
Leu Thr Leu Ile Phe Leu Thr Cys Val Ala Ala Thr Leu Leu Val Ala
      305             310             315             320

```

317

Glu Glu Ala Ala Leu Gly Pro Thr Glu Pro Ala Glu Gly Leu Ser Ala  
                                   325                                  330                                  335  
 Pro Ser Leu Ser Pro His Cys Cys Pro Cys Arg Ala Arg Leu Ala Phe  
                                   340                                  345                                  350  
 Arg Asn Leu Gly Ala Leu Leu Pro Arg Leu His Gln Leu Cys Cys Arg  
                                   355                                  360                                  365  
 Met Pro Arg Thr Leu Arg Arg Leu Phe Val Ala Glu Leu Cys Ser Trp  
                                   370                                  375                                  380  
 Met Ala Leu Met Thr Phe Thr Leu Phe Tyr Thr Asp Phe Val Gly Glu  
                                   385                                  390                                  395                                  400

<210> 853  
 <211> 20  
 <212> PRT  
 <213> Homo sapiens

<400> 853  
 Leu Leu Pro Pro Pro Pro Ala Leu Cys Gly Ala Ser Ala Cys Asp Val  
                                   5                                  10                                  15  
 Ser Val Arg Val  
                                   20

<210> 854  
 <211> 60  
 <212> DNA  
 <213> Homo sapiens

<400> 854  
 ctgctccac ctccaccgc gctctgcggg gcctctgcct gtgatgtctc cgtacgtgtg 60

<210> 855  
 <211> 10  
 <212> PRT  
 <213> Homo sapiens

<400> 855  
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320

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&lt;400&gt; 875

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&lt;211&gt; 9

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 876

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&lt;210&gt; 877

&lt;211&gt; 9

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 877

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&lt;210&gt; 878

&lt;211&gt; 1195

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 878

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&lt;210&gt; 879

&lt;211&gt; 339

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

322

&lt;400&gt; 879

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&lt;210&gt; 880

&lt;211&gt; 2172

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 880

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323

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&lt;210&gt; 881

&lt;211&gt; 2455

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 881

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&lt;211&gt; 2455

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 882

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325

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&lt;210&gt; 883

&lt;211&gt; 62

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 883

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                50                      55                      60

```

&lt;210&gt; 884

&lt;211&gt; 135

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 884

```

Met Val Glu Gly Glu Gly Glu Ala Arg His Val Leu His Gly Gly Arg
                    5                      10                      15
Arg Glu Arg Val Arg Gly Glu Thr Ala Thr Asn Phe Phe Phe Leu Arg
                20                      25                      30
Gln Glu Ser Gly Pro Val Ala Gln Ala Gly Val Gln Trp His Asp Leu
                35                      40                      45
Ser Ser Leu Gln Pro Leu Pro His Arg Phe Lys Gln Phe Ser Cys Leu
                50                      55                      60
Ser Leu Pro His Ser Trp Asp His Arg Tyr Ala Pro Pro His Leu Ala
                65                      70                      75                      80
Asn Phe Cys Ser Phe Ser Arg Asp Gly Val Ser Leu Cys Cys Ser Gly
                85                      90                      95
Trp Ser Lys Thr Pro Gly Leu Gln Gln Ser Ala Cys Leu Gly Leu Pro
                100                      105                      110
Lys Cys Trp Gly Tyr Arg His Lys Pro Pro His Pro Ala Cys His Ile
                115                      120                      125
Leu Leu Asn Tyr Gln Val Ser
                130                      135

```

&lt;210&gt; 885

&lt;211&gt; 77

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 885

```

Met His Tyr His Lys Asn Ser Met Gly Lys Ile Pro Pro Ile Ile Gln

```

326

```

          5          10          15
Ser Pro Pro Thr Arg Ser Pro Pro Thr Arg Gly Ile Gly Trp Gly His
          20          25          30
Arg Ala Lys Pro Tyr Gln Met Leu Gln Gly Leu Gly Thr Leu Arg Pro
          35          40          45
Leu Arg Pro Gly Val Ser Val Thr Leu Leu Gly Ser Val Cys Leu Gln
          50          55          60
Asp Leu Pro Pro Leu Pro Trp Tyr Arg Arg Lys Val Leu
          65          70          75

```

&lt;210&gt; 886

&lt;211&gt; 60

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 886

```

Met Leu Val His Ile Tyr Ser Cys Cys Gly Met Val Tyr Arg Phe Gly
          5          10          15
Gln Met Ser Asp Asn Pro Phe Tyr Ile Leu Ala Ser Leu Gly Ser Ser
          20          25          30
Ser Cys Arg Asn Gly Leu Ala Ser Lys Trp Arg Gln Ala Asp Pro Ser
          35          40          45
Asp Gly Tyr Met Glu Pro Cys Phe Gln Leu Leu Phe
          50          55          60

```

&lt;210&gt; 887

&lt;211&gt; 76

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 887

```

Met Cys Leu Cys Ile Pro Leu Gly Gly Tyr Gln Glu Leu Cys His Cys
          5          10          15
Met Ser Thr Ser Asp Gly Phe Ala Pro Pro Pro Gln Leu Gly Ser Arg
          20          25          30
Cys Ser His Ile Arg Gly Pro Ile Lys Ile Ala Arg Asn Lys Phe Pro
          35          40          45
Arg Thr Leu Thr Ser Gln Glu Leu Arg Arg Phe Ala Glu Tyr Ser Gly
          50          55          60
Met Met Phe Gly Asp Gln Thr Thr Ala Gly Gln Lys
          65          70          75

```

&lt;210&gt; 888

&lt;211&gt; 76

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 888

```

Met Val Lys Ser Arg Phe Thr Lys Asn Thr Lys Ile Thr Gln Ala Trp
          5          10          15
Trp Arg Ala Pro Val Ile Pro Gly Thr Arg Glu Ala Glu Gly Gly Glu
          20          25          30
Ser Leu Glu Pro Gly Arg Leu Arg Glu Glu Asn Arg Leu Asn Pro Gly
          35          40          45
Gly Arg Gly Cys Ser Glu Pro Arg Ser Cys Cys Cys Thr Pro Ala Trp
          50          55          60
Ser Thr Glu Gln Asp Ser Ala Ser Lys Thr Asn Lys
          65          70          75

```

327

<210> 889  
 <211> 80  
 <212> PRT  
 <213> Homo sapiens

<400> 889  
 Met Leu Leu His Ser Ser Leu Val Asn Arg Ala Arg Leu Cys Leu Lys  
                                   5                                  10                                  15  
 Asn Lys Gln Ile Asn Lys Gln Thr Asn Lys Thr Glu Arg Phe Cys Cys  
                                   20                                  25                                  30  
 Asn Val Gln Gly Ala Ile Cys Ser Phe Lys Lys Ile Ile Phe Gly Gln  
                                   35                                  40                                  45  
 Ala Gln Trp Leu Thr Pro Val Ile Pro Ala Leu Trp Glu Ala Lys Val  
                                   50                                  55                                  60  
 Gly Gly Ser Phe Glu Val Arg Ser Leu Arg Ser Ala Trp Pro Thr Trp  
                                   65                                  70                                  75                                  80

<210> 890  
 <211> 72  
 <212> PRT  
 <213> Homo sapiens

<400> 890  
 Met His Tyr His Lys Asn Ser Met Gly Lys Ile Pro Pro His Asn Pro  
                                   5                                  10                                  15  
 Ile Thr Ser His Gln Val Ser Ser Asp Thr Trp Asp Trp Val Gly Thr  
                                   20                                  25                                  30  
 Gln Ser Gln Thr Val Ser Asp Ala Ala Gly Ala Gly Asp Thr Glu Thr  
                                   35                                  40                                  45  
 Thr Gln Thr Trp Cys Leu Cys His Ser Ser Gly Leu Cys Leu Ser Pro  
                                   50                                  55                                  60  
 Gly Pro Pro Ser Pro Ser Met Val  
                                   65                                  70

<210> 891  
 <211> 77  
 <212> PRT  
 <213> Homo sapiens

<400> 891  
 Met His Tyr His Lys Asn Ser Met Gly Lys Ile Pro Pro Ile Ile Gln  
                                   5                                  10                                  15  
 Ser Pro Pro Thr Arg Ser Pro Pro Thr Arg Gly Ile Gly Trp Gly His  
                                   20                                  25                                  30  
 Arg Ala Lys Pro Tyr Gln Met Leu Gln Gly Leu Gly Thr Leu Arg Pro  
                                   35                                  40                                  45  
 Leu Arg Pro Gly Val Ser Val Thr Leu Leu Gly Ser Val Cys Leu Gln  
                                   50                                  55                                  60  
 Asp Leu Pro Pro Leu Pro Trp Tyr Arg Arg Lys Val Leu  
                                   65                                  70                                  75

<210> 892  
 <211> 60  
 <212> PRT  
 <213> Homo sapiens

<400> 892



328

Met Leu Val His Ile Tyr Ser Cys Cys Gly Met Val Tyr Arg Phe Gly  
                                   5                                  10                                  15  
 Gln Met Ser Asp Asn Pro Phe Tyr Ile Leu Ala Ser Leu Gly Ser Ser  
                                   20                                  25                                  30  
 Ser Cys Arg Asn Gly Leu Ala Ser Lys Trp Arg Gln Ala Asp Pro Ser  
                                   35                                  40                                  45  
 Asp Gly Tyr Met Glu Pro Cys Phe Gln Leu Leu Phe  
                                   50                                  55                                  60

&lt;210&gt; 893

&lt;211&gt; 76

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 893

Met Cys Leu Cys Ile Pro Leu Gly Gly Tyr Gln Glu Leu Cys His Cys  
                                   5                                  10                                  15  
 Met Ser Thr Ser Asp Gly Phe Ala Pro Pro Pro Gln Leu Gly Ser Arg  
                                   20                                  25                                  30  
 Cys Ser His Ile Arg Gly Pro Ile Lys Ile Ala Arg Asn Lys Phe Pro  
                                   35                                  40                                  45  
 Arg Thr Leu Thr Ser Gln Glu Leu Arg Arg Phe Ala Glu Tyr Ser Gly  
                                   50                                  55                                  60  
 Met Met Phe Gly Asp Gln Thr Thr Ala Gly Gln Lys  
                                   65                                  70                                  75

&lt;210&gt; 894

&lt;211&gt; 2479

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 894

gtcatattga acattccaga tacctatcat tactcgatgc tgttgataac agcaagatgg 60  
 ctttgaactc aggggtcacca ccagctattg gaccttacta tgaaaacccat ggataccaac 120  
 cggaaaaccc ctatcccgcga cagcccactg tgggtcccccac tgtctacgag gtgcatccgg 180  
 ctacgtacta cccgtccccc gtgccccagt acgccccgag ggtcctgacg caggcttcca 240  
 acccgcgtcg ctgcacgcag cccaaatccc catccgggac agtgtgcacc tcaaagacta 300  
 agaaagcact gtgcatcacc ttgaccctgg ggaccttcct cgtgggagct gcgctggccg 360  
 ctggcctact ctggaagttc atgggcagca agtgcctcaa ctctgggata gagtgcgact 420  
 cctcaggtac ctgcatcaac ccctctaact ggtgtgatgg cgtgtcacac tgccccggcg 480  
 gggaggcaga gaatcggtgt gttgcctctc acggaccaaa cttcatcctt cagatgtact 540  
 catctcagag gaagtctgtg caccctgtgt gccaaagacga ctggaacgag aactacgggc 600  
 gggcggcctg cagggacatg ggctataaga ataattttta ctctagccaa ggaatagtgg 660  
 atgacagcgg atccaccagc tttatgaaac tgaacacaag tgccggcaat gtcgatatct 720  
 ataaaaaact gtaccacagt gatgcctgtt cttcaaaaagc agtgggtttct ttacgctggt 780  
 tagcctgcgg ggtcaacttg aactcaagcc gccagagcag gatcgtgggc ggtgagagcg 840  
 cgctcccggg ggcctggccc tggcaggtca gcctgcacgt ccagaacgtc cacgtgtgcg 900  
 gaggctccat catcaccccc gagtggatcg tgacagccgc ccactgcgtg gaaaaacctc 960  
 ttaaccaatcc atggcatttg acggcatttg cggggatttt gagacaatct ttcattgtct 1020  
 atggagccgg ataccaagta caaaaagtga tttctcatcc aaattatgac tccaagacca 1080  
 agaacaatga cattgcgctg atgaagctgc agaagcctct gactttcaac gacctagtga 1140  
 aaccagtgtg tctgcccac ccaggcatga tgctgcagcc agaacagctc tgctggattt 1200  
 ccgggtgggg ggccaccgag gagaaaggga agacctcaga agtgcgtgaac gctgccaagg 1260  
 tgctttctcat tgagacacag agatgcaaca gcagatatgt ctatgacaac ctgatcacac 1320  
 cagccatgat ctgtgccggc ttctgtcagg ggaacgtcga ttcttgccag ggtgacagtg 1380  
 gagggcctct ggtcacttcg aacaacaata tctggtggct gataggggat acaagctggg 1440  
 gttctggtcg tgccaaagct tacagaccag gagtgtacgg gaatgtgatg gtattcacgg 1500  
 actggattta tcgacaaatg aaggcaaacg gctaattccac atgggtcttcg tccttgacgt 1560

329

```

cgttttacaa gaaaacaatg gggctgggtt tgcttccccg tgcattgattt actcttagag 1620
atgattcaga ggtcacttca tttttattaa acagtgaact tgtctggctt tggcactctc 1680
tgccatactg tgcaggctgc agtggctccc ctgcccagcc tgctctccct aacccttgt 1740
ccgcaagggg tgatggccgg ctggttggtg gcactggcgg tcaattgtgg aaggaagagg 1800
gttggaggct gccccattg agatcttcct gctgagtcct ttccaggggc caattttgga 1860
tgagcatgga gctgtcactt ctcagctgct ggatgacttg agatgaaaaa ggagagacat 1920
ggaaagggag acagccaggt ggcacctgca ggggctgccc tctggggcca cttggtagt 1980
tccccagcct acttcacaag gggattttgc tgatgggttc ttagagcctt agcagccctg 2040
gatggtggcc agaaataaag ggaccagccc ttcattgggtg gtgacgtggg agtcacttgt 2100
aaggggaaca gaaacatttt tgttcttatg gggtgagaat atagacagtg cccttgggtg 2160
gaggggaagca attgaaaagg aacttgccct gagcactcct ggtgcaggtc tccacctgca 2220
cattgggtgg ggtcctctgg agggagactc agccttcctc ctcactctcc ctgacctgac 2280
tcctagcacc ctggagagtg aatgcccctt ggtccctggc agggcgccaa gtttggcacc 2340
atgtcggcct cttcaggcct gatagtcatt ggaaattgag gtccatgggg gaaatcaagg 2400
atgctcagtt taaggtaacac tgtttccatg ttatgtttct acacattgat ggtggtgacc 2460
ctgagttcaa agccatctt
2479

```

&lt;210&gt; 895

&lt;211&gt; 492

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 895

```

Met Ala Leu Asn Ser Gly Ser Pro Pro Ala Ile Gly Pro Tyr Tyr Glu
      5      10      15
Asn His Gly Tyr Gln Pro Glu Asn Pro Tyr Pro Ala Gln Pro Thr Val
      20      25      30
Val Pro Thr Val Tyr Glu Val His Pro Ala Gln Tyr Tyr Pro Ser Pro
      35      40      45
Val Pro Gln Tyr Ala Pro Arg Val Leu Thr Gln Ala Ser Asn Pro Val
      50      55      60
Val Cys Thr Gln Pro Lys Ser Pro Ser Gly Thr Val Cys Thr Ser Lys
      65      70      75      80
Thr Lys Lys Ala Leu Cys Ile Thr Leu Thr Leu Gly Thr Phe Leu Val
      85      90      95
Gly Ala Ala Leu Ala Ala Gly Leu Leu Trp Lys Phe Met Gly Ser Lys
      100      105      110
Cys Ser Asn Ser Gly Ile Glu Cys Asp Ser Ser Gly Thr Cys Ile Asn
      115      120      125
Pro Ser Asn Trp Cys Asp Gly Val Ser His Cys Pro Gly Gly Glu Asp
      130      135      140
Glu Asn Arg Cys Val Arg Leu Tyr Gly Pro Asn Phe Ile Leu Gln Met
      145      150      155      160
Tyr Ser Ser Gln Arg Lys Ser Trp His Pro Val Cys Gln Asp Asp Trp
      165      170      175
Asn Glu Asn Tyr Gly Arg Ala Ala Cys Arg Asp Met Gly Tyr Lys Asn
      180      185      190
Asn Phe Tyr Ser Ser Gln Gly Ile Val Asp Asp Ser Gly Ser Thr Ser
      195      200      205
Phe Met Lys Leu Asn Thr Ser Ala Gly Asn Val Asp Ile Tyr Lys Lys
      210      215      220
Leu Tyr His Ser Asp Ala Cys Ser Ser Lys Ala Val Val Ser Leu Arg
      225      230      235      240
Cys Leu Ala Cys Gly Val Asn Leu Asn Ser Ser Arg Gln Ser Arg Ile
      245      250      255
Val Gly Gly Glu Ser Ala Leu Pro Gly Ala Trp Pro Trp Gln Val Ser
      260      265      270
Leu His Val Gln Asn Val His Val Cys Gly Gly Ser Ile Ile Thr Pro

```

330

275		280		285
Glu Trp Ile Val Thr Ala Ala His Cys Val Glu Lys Pro Leu Asn Asn				
290		295		300
Pro Trp His Trp Thr Ala Phe Ala Gly Ile Leu Arg Gln Ser Phe Met				
305		310		315
Phe Tyr Gly Ala Gly Tyr Gln Val Gln Lys Val Ile Ser His Pro Asn				
	325		330	335
Tyr Asp Ser Lys Thr Lys Asn Asn Asp Ile Ala Leu Met Lys Leu Gln				
	340		345	350
Lys Pro Leu Thr Phe Asn Asp Leu Val Lys Pro Val Cys Leu Pro Asn				
	355		360	365
Pro Gly Met Met Leu Gln Pro Glu Gln Leu Cys Trp Ile Ser Gly Trp				
	370		375	380
Gly Ala Thr Glu Glu Lys Gly Lys Thr Ser Glu Val Leu Asn Ala Ala				
385		390		395
Lys Val Leu Leu Ile Glu Thr Gln Arg Cys Asn Ser Arg Tyr Val Tyr				
	405		410	415
Asp Asn Leu Ile Thr Pro Ala Met Ile Cys Ala Gly Phe Leu Gln Gly				
	420		425	430
Asn Val Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Thr Ser				
	435		440	445
Asn Asn Asn Ile Trp Trp Leu Ile Gly Asp Thr Ser Trp Gly Ser Gly				
	450		455	460
Cys Ala Lys Ala Tyr Arg Pro Gly Val Tyr Gly Asn Val Met Val Phe				
465		470		475
Thr Asp Trp Ile Tyr Arg Gln Met Lys Ala Asn Gly				
	485		490	

&lt;210&gt; 896

&lt;211&gt; 683

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 896

```

gtcatattga acattccaga tacctatcat tactcgatgc tgttgataac agcaagatgg 60
ctttgaactc agggtcacca ccagctattg gaccttacta tgaaaaccat ggataccaac 120
cggaaaaccc ctatcccgcg cagcccactg tgggtccccc tgtctacgag gtgcatccgg 180
ctcagtacta cccgtccccc gtgccccagt acgccccgag ggtcctgacg caggcttcca 240
accccgctcg ctgcacgcag cccaaatccc catccgggac agtgtgcacc tcaaagacta 300
agaaagcact gtgcatcacc ttgaccctgg ggaccttcct cgtgggagct gcgctggccg 360
ctggcctact ctggaagtgc atgggcagca agtgcctcaa ctctgggata gagtgcgact 420
cctcaggtac ctgcatcaac cctctaaact ggtgtgatgg cgtgtcacac tgccccggcg 480
gggaggacga gaatcggtgt gttcgctctt acggacccaa cttcatcctt cagatgtact 540
catctcagag gaagtctctg caccctgtgt gccaaagcga ctggaacgag aactacgggc 600
gggcggcctg caggacatg ggctataaga ataattttta ctctagccaa ggaatagtgg 660
atgacagcgg atccaccagc ttt                                     683

```

&lt;210&gt; 897

&lt;211&gt; 209

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 897

```

Met Ala Leu Asn Ser Gly Ser Pro Pro Ala Ile Gly Pro Tyr Tyr Glu
1           5           10           15

```

331

```

Asn His Gly Tyr Gln Pro Glu Asn Pro Tyr Pro Ala Gln Pro Thr Val
      20      25      30
Val Pro Thr Val Tyr Glu Val His Pro Ala Gln Tyr Tyr Pro Ser Pro
      35      40      45
Val Pro Gln Tyr Ala Pro Arg Val Leu Thr Gln Ala Ser Asn Pro Val
      50      55      60
Val Cys Thr Gln Pro Lys Ser Pro Ser Gly Thr Val Cys Thr Ser Lys
      65      70      75      80
Thr Lys Lys Ala Leu Cys Ile Thr Leu Thr Leu Gly Thr Phe Leu Val
      85      90      95
Gly Ala Ala Leu Ala Ala Gly Leu Leu Trp Lys Phe Met Gly Ser Lys
      100      105      110
Cys Ser Asn Ser Gly Ile Glu Cys Asp Ser Ser Gly Thr Cys Ile Asn
      115      120      125
Pro Ser Asn Trp Cys Asp Gly Val Ser His Cys Pro Gly Gly Glu Asp
      130      135      140
Glu Asn Arg Cys Val Arg Leu Tyr Gly Pro Asn Phe Ile Leu Gln Met
      145      150      155      160
Tyr Ser Ser Gln Arg Lys Ser Trp His Pro Val Cys Gln Asp Asp Trp
      165      170      175
Asn Glu Asn Tyr Gly Arg Ala Ala Cys Arg Asp Met Gly Tyr Lys Asn
      180      185      190
Asn Phe Tyr Ser Ser Gln Gly Ile Val Asp Asp Ser Gly Ser Thr Ser
      195      200      205
Phe

```

<210> 898  
 <211> 27  
 <212> PRT  
 <213> Homo sapiens

```

<400> 898
Val Gly Glu Gly Leu Tyr Gln Gly Val Pro Arg Ala Glu Pro Gly Thr
  1           5           10           15
Glu Ala Arg Arg His Tyr Asp Glu Gly Val Arg
      20      25

```

<210> 899  
 <211> 35  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> PCR primer

<400> 899  
 ggatccgccg ccaccatgtc actttctagc ctgct

35

<210> 900  
 <211> 27  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> PCR primer

<400> 900

332

gtcgactcag ctggaccaca gccgcag

27

&lt;210&gt; 901

&lt;211&gt; 34

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; PCR primer

&lt;400&gt; 901

ggatccgccg ccaccatggg ctgcaggctg ctct

34

&lt;210&gt; 902

&lt;211&gt; 27

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; PCR primer

&lt;400&gt; 902

gtcgactcag aaatcctttc tcttgac

27

&lt;210&gt; 903

&lt;211&gt; 936

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...()

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 903

atgggctgca	ggctgntctg	ctgtgcgggt	ctctgtctcc	tgggagcgg	ccccatggaa	60
acgggagtta	cgcagacacc	aagacacctg	gtcatgggaa	tgacaaataa	gaagtctttg	120
aaatgtgaac	aacatctggg	tcataacgct	atgtattgg	acaagcaaag	tgctaagaag	180
ccactggagc	tcatgtttgt	ctacagtctt	gaagaacggg	ttgaaaacaa	cagtgtgcca	240
agtcgcttct	cacctgaatg	ccccaacagc	tctcaattat	tccttcacct	acacaccctg	300
cagccagaag	actcggccct	gtatctctgc	gccagcagcc	aagaccggac	aagcagctcc	360
tacgagcagt	acttcgggcc	gggcaccagg	ctcacggcca	cagaggacct	gaaaaacgtg	420
ttcccacccg	aggtcgctgt	gtttgagcca	tcagaagcag	agatctccca	cacccaaaag	480
gccacactgg	tgtgcctggc	cacaggcttc	taccccgacc	acgtggagct	gagctggtgg	540
gtgaatggga	aggaggtgca	cagtggggtc	agcacagacc	cgcagcccct	caaggagcag	600
cccgccctca	atgactccag	atactgcctg	agcagccgcc	tgaggggtctc	ggccaccttc	660
tggcagaacc	cccgaacca	cttcgcgtgt	caagtccagt	tctacgggct	ctcggagaat	720
gacgagtgga	cccaggatag	ggccaaacct	gtcaccaga	tcgtcagcgc	cgaggcctgg	780
ggtagagcag	actgtggctt	cacctccgag	tcttaccagc	aaggggtcct	gtctgccacc	840
atcctctatg	agatcttgc	agggaaggcc	accttgtatg	ccgtgctgg	cagtgccttc	900
gtgctgatgg	ccatgggtcaa	gagaaaggat	ttctga			936

&lt;210&gt; 904

&lt;211&gt; 834

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

333

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...()

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 904

```

atgtcacttt ctagcctgct naaggtgggc acagcttcac tgtggctagg acctggcatt 60
gccagaaga taactcaaac ccaaccagga atgttcgtgc aggaaaagga ggctgtgact 120
ctggactgca catatgacac cagtgatcaa agttatggtc tcttctggta caagcagccc 180
agcagtgagg aaatgatttt tcttatttat caggggtctt atgacgagca aaatgcaaca 240
gaaggtcgct actcattgaa tttccagaag gcaagaaaat ccgccaacct tgtcatctcc 300
gcttcacaac tgggggactc agcaatgtat ttctgtgcaa tgagagaggg cgcgggagga 360
ggaaacaaac tcacctttgg gacaggcact cagctaaaag tggaactcaa tatccagaac 420
cctgaccctg ccgtgtacca gctgagagac tctaaatcca gtgacaagtc tgtctgccta 480
ttcacccgatt ttgattctca aacaaatgtg tcacaaagta aggattctga tgtgtatatc 540
acagacaaaa ctgtgctaga catgaggtct atggacttca agagcaacag tgctgtggcc 600
tgagagcaaca aatctgactt tgcattgtga aacgccttca acaacagcat tattccagaa 660
gacaccttct tccccagccc agaaagtccc tgtgatgtca agctggctga gaaaagcttt 720
gaaacagata cgaacctaaa ctttcaaaac ctgtcagtga ttgggttccg aatcctcctc 780
ctgaaagtgg ccgggtttaa tctgctcatg acgctgcggc tgtggtccag ctga 834

```

&lt;210&gt; 905

&lt;211&gt; 311

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; variant

&lt;222&gt; (1)...(311)

&lt;223&gt; Xaa = Any amino acid

&lt;400&gt; 905

```

Met Gly Cys Arg Leu Xaa Cys Cys Ala Val Leu Cys Leu Leu Gly Ala
      5      10      15
Val Pro Met Glu Thr Gly Val Thr Gln Thr Pro Arg His Leu Val Met
      20      25      30
Gly Met Thr Asn Lys Lys Ser Leu Lys Cys Glu Gln His Leu Gly His
      35      40      45
Asn Ala Met Tyr Trp Tyr Lys Gln Ser Ala Lys Lys Pro Leu Glu Leu
      50      55      60
Met Phe Val Tyr Ser Leu Glu Glu Arg Val Glu Asn Asn Ser Val Pro
      65      70      75      80
Ser Arg Phe Ser Pro Glu Cys Pro Asn Ser Ser His Leu Phe Leu His
      85      90      95
Leu His Thr Leu Gln Pro Glu Asp Ser Ala Leu Tyr Leu Cys Ala Ser
      100     105     110
Ser Gln Asp Arg Thr Ser Ser Ser Tyr Glu Gln Tyr Phe Gly Pro Gly
      115     120     125
Thr Arg Leu Thr Val Thr Glu Asp Leu Lys Asn Val Phe Pro Pro Glu
      130     135     140
Val Ala Val Phe Glu Pro Ser Glu Ala Glu Ile Ser His Thr Gln Lys
      145     150     155     160
Ala Thr Leu Val Cys Leu Ala Thr Gly Phe Tyr Pro Asp His Val Glu
      165     170     175
Leu Ser Trp Trp Val Asn Gly Lys Glu Val His Ser Gly Val Ser Thr
      180     185     190
Asp Pro Gln Pro Leu Lys Glu Gln Pro Ala Leu Asn Asp Ser Arg Tyr
      195     200     205

```

334

Cys Leu Ser Ser Arg Leu Arg Val Ser Ala Thr Phe Trp Gln Asn Pro  
 210 215 220  
 Arg Asn His Phe Arg Cys Gln Val Gln Phe Tyr Gly Leu Ser Glu Asn  
 225 230 235 240  
 Asp Glu Trp Thr Gln Asp Arg Ala Lys Pro Val Thr Gln Ile Val Ser  
 245 250 255  
 Ala Glu Ala Trp Gly Arg Ala Asp Cys Gly Phe Thr Ser Glu Ser Tyr  
 260 265 270  
 Gln Gln Gly Val Leu Ser Ala Thr Ile Leu Tyr Glu Ile Leu Leu Gly  
 275 280 285  
 Lys Ala Thr Leu Tyr Ala Val Leu Val Ser Ala Leu Val Leu Met Ala  
 290 295 300  
 Met Val Lys Arg Lys Asp Phe  
 305 310

&lt;210&gt; 906

&lt;211&gt; 277

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 906

Met Ser Leu Ser Ser Leu Leu Lys Val Val Thr Ala Ser Leu Trp Leu  
 5 10 15  
 Gly Pro Gly Ile Ala Gln Lys Ile Thr Gln Thr Gln Pro Gly Met Phe  
 20 25 30  
 Val Gln Glu Lys Glu Ala Val Thr Leu Asp Cys Thr Tyr Asp Thr Ser  
 35 40 45  
 Asp Gln Ser Tyr Gly Leu Phe Trp Tyr Lys Gln Pro Ser Ser Gly Glu  
 50 55 60  
 Met Ile Phe Leu Ile Tyr Gln Gly Ser Tyr Asp Glu Gln Asn Ala Thr  
 65 70 75 80  
 Glu Gly Arg Tyr Ser Leu Asn Phe Gln Lys Ala Arg Lys Ser Ala Asn  
 85 90 95  
 Leu Val Ile Ser Ala Ser Gln Leu Gly Asp Ser Ala Met Tyr Phe Cys  
 100 105 110  
 Ala Met Arg Glu Gly Ala Gly Gly Gly Asn Lys Leu Thr Phe Gly Thr  
 115 120 125  
 Gly Thr Gln Leu Lys Val Glu Leu Asn Ile Gln Asn Pro Asp Pro Ala  
 130 135 140  
 Val Tyr Gln Leu Arg Asp Ser Lys Ser Ser Asp Lys Ser Val Cys Leu  
 145 150 155 160  
 Phe Thr Asp Phe Asp Ser Gln Thr Asn Val Ser Gln Ser Lys Asp Ser  
 165 170 175  
 Asp Val Tyr Ile Thr Asp Lys Thr Val Leu Asp Met Arg Ser Met Asp  
 180 185 190  
 Phe Lys Ser Asn Ser Ala Val Ala Trp Ser Asn Lys Ser Asp Phe Ala  
 195 200 205  
 Cys Ala Asn Ala Phe Asn Asn Ser Ile Ile Pro Glu Asp Thr Phe Phe  
 210 215 220  
 Pro Ser Pro Glu Ser Ser Cys Asp Val Lys Leu Val Glu Lys Ser Phe  
 225 230 235 240  
 Glu Thr Asp Thr Asn Leu Asn Phe Gln Asn Leu Ser Val Ile Gly Phe  
 245 250 255  
 Arg Ile Leu Leu Leu Lys Val Ala Gly Phe Asn Leu Leu Met Thr Leu  
 260 265 270  
 Arg Leu Trp Ser Ser  
 275

<210> 907  
 <211> 1536  
 <212> DNA  
 <213> Homo sapiens

<400> 907  
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 gtgcccatac accaggggtct caccocctttc aagctggctg gactggaggg taacactgtg 120  
 atgtttcagc acctgatgca gaagcggaag cacaccaggt ggacgtatgg accactgacc 180  
 tcgactctct atgacctcac agagatcgac tcctcagggg atgagcagtc cctgctggaa 240  
 cttatcatca ccaccaagaa gcgggaggct cgccagatcc tggaccagac gccggtgaag 300  
 gagctggtga gcctcaagtg gaagcggtag gggcgccgt acttctgcat gctgggtgcc 360  
 atatatctgc tgtacatcat ctgcttcacc atgtgctgca tctaccgccc cctcaagccc 420  
 aggaccaata accgcacgag ccccggggac aacaccctct tacagcagaa gctacttcag 480  
 gaagcctaca tgaccocctaa ggacgatata cggctggctg gggagctggt gactgtcatt 540  
 ggggctatca tcatcctgct ggtagagggt ccagacatct tcagaatggg ggtcactcgc 600  
 ttctttggac agaccatcct tgggggcccc ttccatgtcc tcatcatcac ctatgccttc 660  
 atggtgctgg tgaccatggt gatgcggctc atcagtcca gcggggaggt ggtacccatg 720  
 tcctttgcac tcgtgctggg ctggtgcaac gtcattgtact tcgcccagg attccagatg 780  
 ctaggccctc tcaccatcat gattcagaag atgatttttg gcgacctgat gcgattctgc 840  
 tggctgatgg ctgtggtcat cctgggcttt gcttcagcct tctatatcat cttccagaca 900  
 gaggaccccg aggagctagg ccacttctac gactaccca tggccctgtt cagcaccttc 960  
 gagctgttcc ttaccatcat cgatggcccc gccaaactaca acgtggacct gcccttcatt 1020  
 tacagcatca cctatgctgc ctttgccatc atcgccacac tgctcatgct caacctcctc 1080  
 attgccatga tgggcgacac tcaactggcga gtggcccatg agcgggatga gctgtggagg 1140  
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 cgctccggga tctgcggacg ggagtatggc ctgggagacc gctggttcct gcgggtggaa 1260  
 gacaggcaag atctcaaccg gcagcggatc caacgctacg cacaggcctt ccacaccg 1320  
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 cccacactgt cccttcctat gccctcagtg tctcgaagta cctcccgag cagtccaat 1440  
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 ctggaggacg gggagagctg ggaatatcag atctga 1536

<210> 908  
 <211> 1533  
 <212> DNA  
 <213> Homo sapiens

<400> 908  
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 atgtttcagc acctgatgca gaagcggaag cacaccaggt ggacgtatgg accactgacc 180  
 tcgactctct atgacctcac agagatcgac tcctcagggg atgagcagtc cctgctggaa 240  
 cttatcatca ccaccaagaa gcgggaggct cgccagatcc tggaccagac gccggtgaag 300  
 gagctggtga gcctcaagtg gaagcggtag gggcgccgt acttctgcat gctgggtgcc 360  
 atatatctgc tgtacatcat ctgcttcacc atgtgctgca tctaccgccc cctcaagccc 420  
 aggaccaata accgcacgag ccccggggac aacaccctct tacagcagaa gctacttcag 480  
 gaagcctaca tgaccocctaa ggacgatata cggctggctg gggagctggt gactgtcatt 540  
 ggggctatca tcatcctgct ggtagagggt ccagacatct tcagaatggg ggtcactcgc 600  
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 atggtgctgg tgaccatggt gatgcggctc atcagtcca gcggggaggt ggtacccatg 720  
 tcctttgcac tcgtgctggg ctggtgcaac gtcattgtact tcgcccagg attccagatg 780  
 ctaggccctc tcaccatcat gattcagaag atgatttttg gcgacctgat gcgattctgc 840  
 tggctgatgg ctgtggtcat cctgggcttt gcttcagcct tctatatcat cttccagaca 900  
 gaggaccccg aggagctagg ccacttctac gactaccca tggccctgtt cagcaccttc 960  
 gagctgttcc ttaccatcat cgatggcccc gccaaactaca acgtggacct gcccttcatt 1020  
 tacagcatca cctatgctgc ctttgccatc atcgccacac tgctcatgct caacctcctc 1080



336

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attgccatga tgggcgacac tcaactggcga gtggcccatg agcgggatga gctgtggagg 1140
gccagattg tggccaccac ggtgatgctg gagcgggaagc tgcctcgctg cctgtggcct 1200
cgctccggga tctgcggaag ggagtatggc ctgggagacc gctgggttct gcgggtggaa 1260
gacaggcaag atctcaaccg gcagcggatc caacgctacg cacaggcctt ccacacccgg 1320
ggctctgagg atttgacaa agactcagtg gaaaaactag agctgggctg tcccttcagc 1380
ccccacctgt cccttcctat gccctcagtg tctogaagta cctccgcag cagtgcgaat 1440
tgggaaaggc ttccggaagg gaccctgagg agagacctgc gtgggataat caacaggggt 1500
ctggaggacg gggagagctg ggaatatcag atc 1533

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&lt;210&gt; 909

&lt;211&gt; 511

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 909

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Met Tyr Asn Leu Leu Leu Ser Tyr Asp Arg His Gly Asp His Leu Gln
                    5              10              15
Pro Leu Asp Leu Val Pro Asn His Gln Gly Leu Thr Pro Phe Lys Leu
          20              25              30
Ala Gly Val Glu Gly Asn Thr Val Met Phe Gln His Leu Met Gln Lys
          35              40              45
Arg Lys His Thr Gln Trp Thr Tyr Gly Pro Leu Thr Ser Thr Leu Tyr
          50              55              60
Asp Leu Thr Glu Ile Asp Ser Ser Gly Asp Glu Gln Ser Leu Leu Glu
          65              70              75
Leu Ile Ile Thr Thr Lys Lys Arg Glu Ala Arg Gln Ile Leu Asp Gln
          85              90              95
Thr Pro Val Lys Glu Leu Val Ser Leu Lys Trp Lys Arg Tyr Gly Arg
          100             105             110
Pro Tyr Phe Cys Met Leu Gly Ala Ile Tyr Leu Leu Tyr Ile Ile Cys
          115             120             125
Phe Thr Met Cys Cys Ile Tyr Arg Pro Leu Lys Pro Arg Thr Asn Asn
          130             135             140
Arg Thr Ser Pro Arg Asp Asn Thr Leu Leu Gln Gln Lys Leu Leu Gln
          145             150             155
Glu Ala Tyr Met Thr Pro Lys Asp Asp Ile Arg Leu Val Gly Glu Leu
          165             170             175
Val Thr Val Ile Gly Ala Ile Ile Ile Leu Leu Val Glu Val Pro Asp
          180             185             190
Ile Phe Arg Met Gly Val Thr Arg Phe Phe Gly Gln Thr Ile Leu Gly
          195             200             205
Gly Pro Phe His Val Leu Ile Ile Thr Tyr Ala Phe Met Val Leu Val
          210             215             220
Thr Met Val Met Arg Leu Ile Ser Ala Ser Gly Glu Val Val Pro Met
          225             230             235
Ser Phe Ala Leu Val Leu Gly Trp Cys Asn Val Met Tyr Phe Ala Arg
          245             250             255
Gly Phe Gln Met Leu Gly Pro Phe Thr Ile Met Ile Gln Lys Met Ile
          260             265             270
Phe Gly Asp Leu Met Arg Phe Cys Trp Leu Met Ala Val Val Ile Leu
          275             280             285
Gly Phe Ala Ser Ala Phe Tyr Ile Ile Phe Gln Thr Glu Asp Pro Glu
          290             295             300
Glu Leu Gly His Phe Tyr Asp Tyr Pro Met Ala Leu Phe Ser Thr Phe
          305             310             315
Glu Leu Phe Leu Thr Ile Ile Asp Gly Pro Ala Asn Tyr Asn Val Asp
          325             330             335
Leu Pro Phe Met Tyr Ser Ile Thr Tyr Ala Ala Phe Ala Ile Ile Ala

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337

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          340          345          350
Thr Leu Leu Met Leu Asn Leu Leu Ile Ala Met Met Gly Asp Thr His
          355          360          365
Trp Arg Val Ala His Glu Arg Asp Glu Leu Trp Arg Ala Gln Ile Val
          370          375          380
Ala Thr Thr Val Met Leu Glu Arg Lys Leu Pro Arg Cys Leu Trp Pro
385          390          395          400
Arg Ser Gly Ile Cys Gly Arg Glu Tyr Gly Leu Gly Asp Arg Trp Phe
          405          410          415
Leu Arg Val Glu Asp Arg Gln Asp Leu Asn Arg Gln Arg Ile Gln Arg
          420          425          430
Tyr Ala Gln Ala Phe His Thr Arg Gly Ser Glu Asp Leu Asp Lys Asp
          435          440          445
Ser Val Glu Lys Leu Glu Leu Gly Cys Pro Phe Ser Pro His Leu Ser
          450          455          460
Leu Pro Met Pro Ser Val Ser Arg Ser Thr Ser Arg Ser Ser Ala Asn
465          470          475          480
Trp Glu Arg Leu Arg Gln Gly Thr Leu Arg Arg Asp Leu Arg Gly Ile
          485          490          495
Ile Asn Arg Gly Leu Glu Asp Gly Glu Ser Trp Glu Tyr Gln Ile
          500          505          510

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&lt;210&gt; 910

&lt;211&gt; 134

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 910

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Met Tyr Asn Leu Leu Leu Ser Tyr Asp Arg His Gly Asp His Leu Gln
          5          10          15
Pro Leu Asp Leu Val Pro Asn His Gln Gly Leu Thr Pro Phe Lys Leu
          20          25          30
Ala Gly Val Glu Gly Asn Thr Val Met Phe Gln His Leu Met Gln Lys
          35          40          45
Arg Lys His Thr Gln Trp Thr Tyr Gly Pro Leu Thr Ser Thr Leu Tyr
          50          55          60
Asp Leu Thr Glu Ile Asp Ser Ser Gly Asp Glu Gln Ser Leu Leu Glu
          65          70          75          80
Leu Ile Ile Thr Thr Lys Lys Arg Glu Ala Arg Gln Ile Leu Asp Gln
          85          90          95
Thr Pro Val Lys Glu Leu Val Ser Leu Lys Trp Lys Arg Tyr Gly Arg
          100          105          110
Pro Tyr Phe Cys Met Leu Gly Ala Ile Tyr Leu Leu Tyr Ile Ile Cys
          115          120          125
Phe Thr Met Cys Cys Ile
          130

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&lt;210&gt; 911

&lt;211&gt; 55

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 911

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Ala Tyr Arg Pro Leu Lys Pro Arg Thr Asn Asn Arg Thr Ser Pro Arg
          5          10          15
Asp Asn Thr Leu Leu Gln Gln Lys Leu Leu Gln Glu Ala Tyr Met Thr
          20          25          30
Pro Lys Asp Asp Ile Arg Leu Val Gly Glu Leu Val Thr Val Ile Gly

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338

35 40 45  
 Ala Ile Ile Ile Leu Leu Val  
 50 55

<210> 912  
 <211> 39  
 <212> PRT  
 <213> Homo sapiens

<400> 912  
 Glu Val Pro Asp Ile Phe Arg Met Gly Val Thr Arg Phe Phe Gly Gln  
 5 10 15  
 Thr Ile Leu Gly Gly Pro Phe His Val Leu Ile Ile Thr Tyr Ala Phe  
 20 25 30  
 Met Val Leu Val Thr Met Val  
 35

<210> 913  
 <211> 19  
 <212> PRT  
 <213> Homo sapiens

<400> 913  
 Met Arg Leu Ile Ser Ala Ser Gly Glu Val Val Pro Met Ser Phe Ala  
 5 10 15  
 Leu Val Leu

<210> 914  
 <211> 52  
 <212> PRT  
 <213> Homo sapiens

<400> 914  
 Gly Trp Cys Asn Val Met Tyr Phe Ala Arg Gly Phe Gln Met Leu Gly  
 5 10 15  
 Pro Phe Thr Ile Met Ile Gln Lys Met Ile Phe Gly Asp Leu Met Arg  
 20 25 30  
 Phe Cys Trp Leu Met Ala Val Val Ile Leu Gly Phe Ala Ser Ala Phe  
 35 40 45  
 Tyr Ile Ile Phe  
 50

<210> 915  
 <211> 213  
 <212> PRT  
 <213> Homo sapiens

<400> 915  
 Gln Thr Glu Asp Pro Glu Glu Leu Gly His Phe Tyr Asp Tyr Pro Met  
 5 10 15  
 Ala Leu Phe Ser Thr Phe Glu Leu Phe Leu Thr Ile Ile Asp Gly Pro  
 20 25 30  
 Ala Asn Tyr Asn Val Asp Leu Pro Phe Met Tyr Ser Ile Thr Tyr Ala  
 35 40 45  
 Ala Phe Ala Ile Ile Ala Thr Leu Leu Met Leu Asn Leu Leu Ile Ala  
 50 55 60  
 Met Met Gly Asp Thr His Trp Arg Val Ala His Glu Arg Asp Glu Leu

339

65					70					75				80
Trp	Arg	Ala	Gln	Ile	Val	Ala	Thr	Thr	Val	Met	Leu	Glu	Arg	Lys
				85					90					95
Pro	Arg	Cys	Leu	Trp	Pro	Arg	Ser	Gly	Ile	Cys	Gly	Arg	Glu	Tyr
			100					105					110	
Leu	Gly	Asp	Arg	Trp	Phe	Leu	Arg	Val	Glu	Asp	Arg	Gln	Asp	Leu
		115					120					125		Asn
Arg	Gln	Arg	Ile	Gln	Arg	Tyr	Ala	Gln	Ala	Phe	His	Thr	Arg	Gly
		130					135					140		Ser
Glu	Asp	Leu	Asp	Lys	Asp	Ser	Val	Glu	Lys	Leu	Glu	Leu	Gly	Cys
		145				150				155				Pro
Phe	Ser	Pro	His	Leu	Ser	Leu	Pro	Met	Pro	Ser	Val	Ser	Arg	Ser
				165					170					Thr
Ser	Arg	Ser	Ser	Ala	Asn	Trp	Glu	Arg	Leu	Arg	Gln	Gly	Thr	Leu
				180					185					Arg
Arg	Asp	Leu	Arg	Gly	Ile	Ile	Asn	Arg	Gly	Leu	Glu	Asp	Gly	Glu
		195					200					205		Ser
Trp	Glu	Tyr	Gln	Ile										
				210										

&lt;210&gt; 916

&lt;211&gt; 1302

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 916

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ttcatcctaa taggcctccc tggtttagaa gaggtcagc tctgggtggc cttcccattg 180
tgctccctct accttattgc tgtgctaggt aacttgacaa tcatctacat tgtgcggact 240
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ctcatctcca cctcatccat gcccaaatg ctggccatct tctggttcaa ttccactacc 360
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aatatccttt cccattccta ctgcctacac caagatgtca tgaagctggc ctgtgatgat 660
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cccgctcatct tggccaatat ctatctgctg gttcctcctg tgcctcaacc aattgtctat 960
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&lt;210&gt; 917

&lt;211&gt; 2061

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 917

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acgattcgac agcgcacact tcgacttttc catgtggcca cacacgcttc agagccctag 60
gtgtcagtgat tcaaacttct tttccattca gagtcctctg attcagattt taatgttaac 120

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at t t t t g g a a g   a c a g t a t t c a   g a a a a a a a t   t t c c t t a a t a   a a a a t a c a a c   t c a g a t c c t t   180
c a a a t a t g a a   a c t g g t t g g g   g a a t c t c c a t   t t t t t c a a t a   t t a t t t t c t t   c t t t g t t t t c   240
t t g c t a c a t a   t a a t t a t t a a   t a c c c t g a c t   a g g t t g t g g t   t g g a g g g t t a   t t a c t t t t c a   300
t t t t a c c a t g   c a g t c c a a a t   c t a a a c t g c t   t c t a c t g a t g   g t t t a c a g c a   t t c t g a g a t a   360
a g a a t g g t a c   a t c t a g a g a a   c a t t t g c c a a   a g g c c t a a g c   a c g g c a a a g g   a a a a t a a a c a   420
c a g a a t a t a a   t a a a a t g a g a   t a a t c t a g c t   t a a a a c t a t a   a c t t c c t c t t   c a g a a c t c c c   480
a a c c a c a t t g   g a t c t c a g a a   a a a t g c t g t c   t t c a a a a t g a   c t t c t a c a g a   g a a g a a a t a a   540
t t t t t c c t c t   g g a c a c t a g c   a c t t a a g g g g   a a g a t t g g a a   g t a a a g c c t t   g a a a a g a g t a   600
c a t t t a c c t a   c g t t a a t g a a   a g t t g a c a c a   c t g t t c t g a g   a g t t t t c a c a   g c a t a t g g a c   660
c c t g t t t t t c   c t a t t t a a t t   t t c t t a t c a a   c c c t t t a a t t   a g g c a a a g a t   a t t a t t a g t a   720
c c c t c a t t g t   a g c c a t g g g a   a a a t t g a t g t   t c a g t g g g g a   t c a g t g a a t t   a a a t g g g g t c   780
a t a c a a g t a t   a a a a a t t a a a   a a a a a a g g a c   t t c a t g c c c a   a t c t c a t a t g   a t g t g g a a g a   840
a c t g t t a g a g   a g a c c a a c a g   g g t a g t g g g t   t a g a g a t t t c   c a g a g t c t t a   c a t t t t c t a g   900
a g g a g g t a t t   t a a t t t c t t c   t c a c t c a t c c   a g t g t t g t a t   t t a g g a a t t t   c c t g g c a a g   960
g a a c t c a t g g   c t t t a a t c c c   a c t a g c t a t t   g c t t a t t g t c   c t g g t c c a a t   t g c c a a t t a c   1020
c t g t g t c t t g   g a a g a a g t g a   t t t c t a g g t t   c a c c a t t a t g   g a a g a t t c t t   a t t c a g a a a g   1080
t c t g c a t a g g   g c t t a t a g c a   a g t t a t t t a t   t t t t a a a a g t   t c c a t a g g t g   a t t c t g a t a g   1140
g c a g t g a g g t   t a g g g a g c c a   c c a g t t a t g a   t g g g a a g t a t   g g a a t g g c a g   g t c t t g a a g a   1200
t a a c a t t g g c   c t t t t g a g t g   t g a c t c g t a g   c t g g a a a g t g   a g g g a a t c t t   c a g g a c c a t g   1260
c t t t a t t t g g   g g c t t t g t g c   a g t a t g g a a c   a g g g a c t t t g   a g a c c a g g a a   a g c a a t c t g a   1320
c t t a g g c a t g   g g a a t c a g g c   a t t t t t g c t t   c t g a g g g g c t   a t t a c c a a g g   g t t a a t a g g t   1380
t t c a t c t t c a   a c a g g a t a t g   a c a a c a g t g t   t a a c c a a g a a   a c t c a a a t t a   c a a a t a c t a a   1440
a a c a t g t g a t   c a t a t a t g t g   g t a a g t t t c a   t t t t c t t t t t   c a a t c c t c a g   g t t c c c t g a t   1500
a t g g a t t c c t   a t a a c a t g c t   t t c a t c c c c t   t t t g t a a t g g   a t a t c a t a t t   t g g a a t g c c   1560
t a t t t a a t a c   t t g t a t t t g c   t g c t g g a c t g   t a a g c c c a t g   a g g g c a c t g t   t t a t t a t t g a   1620
a t g t c a t c t c   t g t t c a t c a t   t g a c t g c t c t   t t g c t c a t c a   t t g a a t c c c c   c a g c a a a g t g   1680
c c t a g a a c a t   a a t a g t g c t t   a t g c t t g a c a   c c g g t t a t t t   t t c a t c a a a c   c t g a t t c c t t   1740
c t g t c c t g a a   c a c a t a g c c a   g g c a a t t t t c   c a g c c t t c t t   t g a g t t g g g t   a t t a t t a a a t   1800
t c t g g c c a t t   a c t t c c a a t g   t g a g t g g a a g   t g a c a t g t g c   a a t t t c t a t a   c c t g g c t c a t   1860
a a a a c c c t c c   c a t g t g c a g c   c t t t c a t g t t   g a c a t t a a a t   g t g a c t t g g g   a a g c t a t g t g   1920
t t a c a c a g a g   t a a a t c a c c a   g a a g c c t g g a   t t t c t g a a a a   a a c t g t g c a g   a g c c a a a c c t   1980
c t g t c a t t t g   c a a c t c c c a c   t t g t a t t t g t   a c g a g g c a g t   t g g a t a a g t g   a a a a t a a a g   2040
t a c t a t t g t g   t c a a g t c t c t   g

```

&lt;210&gt; 918

&lt;211&gt; 957

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 918

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a t g a t g g t g g   a t c c c a a t g g   c a a t g a a t c c   a g t g c t a c a t   a c t t c a t c c t   a a t a g g c c t c   60
c c t g g t t t a g   a a g a g g c t c a   g t t c t g g t t g   g c c t t c c c a t   t g t g c t c c c t   c t a c c t t a t t   120
g c t g t g c t a g   g t a a c t t g a c   a a t c a t c t a c   a t t g t g c g g a   c t g a g c a c a g   c c t g c a t g a g   180
c c c a t g t a t a   t a t t t c t t t g   c a t g c t t t c a   g g c a t t g a c a   t c c t c a t c t c   c a c c t c a t c c   240
a t g c c c a a a a   t g c t g g c c a t   c t t c t g g t t c   a a t t c c a c t a   c c a t c c a g t t   t g a t g c t t g t   300
c t g c t a c a g a   t g t t t g c c a t   c c a c t c c t t a   t c t g g c a t g g   a a t c c a c a g t   g c t g c t g g c c   360
a t g g c t t t t g   a c c g c t a t g t   g g c c a t c t g t   c a c c c a c t g c   g c c a t g c c a c   a g t a c t t a c g   420
t t g c c t c g t g   t c a c c a a a a t   t g g t g t g g c t   g c t g t g g t g c   g g g g g g c t g c   a c t g a t g g c a   480
c c c c t t c c t g   t c t t c a t c a a   g c a g c t g c c c   t t c t g c c g c t   c c a a t a t c c t   t t c c c a t t c c   540
t a c t c c c t a c   a c c a a g a t g t   c a t g a a g c t g   g c c t g t g a t g   a t a t c c g g g t   c a a t g t c g t c   600
t a t g g c c t t a   t c g t c a t c a t   c t c o g c c a t t   g g c c t g g a c t   c a c t t t c t c a t   c t c c t t c t c a   660
t a t c t g c t t a   t t o t t a a g a c   t g t g t t g g g c   t t g a c a c g t g   a a g c c c a g g c   c a a g g c a t t t   720
g g c a c t t g c g   t c t c t c a t g t   g t g t g c t g t g   t t c a t a t t c t   a t g t a c c t t t   c a t t g g a t t g   780
t c c a t g g t g c   a t c g c t t t a g   c a a g c g g c g t   g a c t c t c c g c   t g c c c g t c a t   c t t g g c c a a t   840
a t c t a t c t g c   t g g t t c c t c c   t g t g c t c a a c   c c a a t t g t c t   a t g g a g t g a a   g a c a a a g g a g   900
a t t c g a c a g c   g c a t c c t t c g   a c t t t t c c a t   g t g g c c a c a c   a c g c t t c a g a   g c c c t a g   957

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&lt;210&gt; 919

341

<211> 954  
 <212> DNA  
 <213> Homo sapiens

<400> 919  
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 gctgtgctag gtaacttgac aatcatctac attgtgogga ctgagcacag cctgcatgag 180  
 cccatgtata tatttctttg catgctttca ggcattgaca tcctcatctc cacctcatcc 240  
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<210> 920  
 <211> 318  
 <212> PRT  
 <213> Homo sapiens

<400> 920  
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                   20                  25                  30  
 Pro Leu Cys Ser Leu Tyr Leu Ile Ala Val Leu Gly Asn Leu Thr Ile  
                   35                  40                  45  
 Ile Tyr Ile Val Arg Thr Glu His Ser Leu His Glu Pro Met Tyr Ile  
                   50                  55                  60  
 Phe Leu Cys Met Leu Ser Gly Ile Asp Ile Leu Ile Ser Thr Ser Ser  
                   65                  70                  75                  80  
 Met Pro Lys Met Leu Ala Ile Phe Trp Phe Asn Ser Thr Thr Ile Gln  
                   85                  90                  95  
 Phe Asp Ala Cys Leu Leu Gln Met Phe Ala Ile His Ser Leu Ser Gly  
                   100                  105                  110  
 Met Glu Ser Thr Val Leu Leu Ala Met Ala Phe Asp Arg Tyr Val Ala  
                   115                  120                  125  
 Ile Cys His Pro Leu Arg His Ala Thr Val Leu Thr Leu Pro Arg Val  
                   130                  135                  140  
 Thr Lys Ile Gly Val Ala Ala Val Val Arg Gly Ala Ala Leu Met Ala  
                   145                  150                  155                  160  
 Pro Leu Pro Val Phe Ile Lys Gln Leu Pro Phe Cys Arg Ser Asn Ile  
                   165                  170                  175  
 Leu Ser His Ser Tyr Cys Leu His Gln Asp Val Met Lys Leu Ala Cys  
                   180                  185                  190  
 Asp Asp Ile Arg Val Asn Val Val Tyr Gly Leu Ile Val Ile Ile Ser  
                   195                  200                  205  
 Ala Ile Gly Leu Asp Ser Leu Leu Ile Ser Phe Ser Tyr Leu Leu Ile  
                   210                  215                  220  
 Leu Lys Thr Val Leu Gly Leu Thr Arg Glu Ala Gln Ala Lys Ala Phe  
                   225                  230                  235                  240

342

Gly	Thr	Cys	Val	Ser	His	Val	Cys	Ala	Val	Phe	Ile	Phe	Tyr	Val	Pro
				245					250					255	
Phe	Ile	Gly	Leu	Ser	Met	Val	His	Arg	Phe	Ser	Lys	Arg	Arg	Asp	Ser
			260					265					270		
Pro	Leu	Pro	Val	Ile	Leu	Ala	Asn	Ile	Tyr	Leu	Leu	Val	Pro	Pro	Val
			275				280					285			
Leu	Asn	Pro	Ile	Val	Tyr	Gly	Val	Lys	Thr	Lys	Glu	Ile	Arg	Gln	Arg
	290					295					300				
Ile	Leu	Arg	Leu	Phe	His	Val	Ala	Thr	His	Ala	Ser	Glu	Pro		
305					310					315					

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<210> 921
<211> 28
<212> PRT
<213> Homo sapiens
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<400> 921
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                20                      25

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<210> 922
<211> 9
<212> PRT
<213> Homo sapiens
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<400> 922  
Arg Thr Glu His Ser Leu His Glu Pro  
5

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<210> 923
<211> 21
<212> PRT
<213> Homo sapiens
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<400> 923
Lys Met Leu Ala Ile Phe Trp Phe Asn Ser Thr Thr Ile Gln Phe Asp
                    5              10              15
Ala Cys Leu Leu Gln
                20

```

```
<210> 924
<211> 20
<212> PRT
<213> Homo sapiens
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```

<400> 924
Asp Arg Tyr Val Ala Ile Cys His Pro Leu Arg His Ala Thr Val Leu
          5              10              15
Thr Leu Pro Arg
          20

```

```
<210> 925
<211> 37
<212> PRT
<213> Homo sapiens
```

343

&lt;400&gt; 925

Phe Ile Lys Gln Leu Pro Phe Cys Arg Ser Asn Ile Leu Ser His Ser  
                           5                          10                          15  
 Tyr Cys Leu His Gln Asp Val Met Lys Leu Ala Cys Asp Asp Ile Arg  
                           20                          25                          30  
 Val Asn Val Val Tyr  
                           35

&lt;210&gt; 926

&lt;211&gt; 13

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 926

Lys Thr Val Leu Gly Leu Thr Arg Glu Ala Gln Ala Lys  
                           5                          10

&lt;210&gt; 927

&lt;211&gt; 10

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 927

Val His Arg Phe Ser Lys Arg Arg Asp Ser  
                           5                          10

&lt;210&gt; 928

&lt;211&gt; 22

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 928

Lys Thr Lys Glu Ile Arg Gln Arg Ile Leu Arg Leu Phe His Val Ala  
                           5                          10                          15

Thr His Ala Ser Glu Pro  
                           20

&lt;210&gt; 929

&lt;211&gt; 3245

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 929

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 gcggggagcg ccgcctggag cgcggcaggt catattgaac attccagata cctatcatta 120  
 ctcgatgctg ttgataacag caagatggct ttgaactcag ggtcaccacc agctattgga 180  
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 gtccccactg tctacgaggt gcatccggct cagtactacc cgtccccgt gccccagtac 300  
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 aatttttact ctagccaagg aatagtggat gacagcggat ccaccagctt tatgaaactg 780



344

```

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gccgc

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3245

&lt;210&gt; 930

&lt;211&gt; 1479

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 930

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atggctttga actcagggtc accaccagct attggacctt actatgaaaa ccatggatac 60
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345

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```

&lt;210&gt; 931

&lt;211&gt; 1476

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 931

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&lt;210&gt; 932

&lt;211&gt; 492

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 932

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Asn	His	Gly	Tyr	Gln	Pro	Glu	Asn	Pro	Tyr	Pro	Ala	Gln	Pro	Thr	Val
			20					25					30		
Val	Pro	Thr	Val	Tyr	Glu	Val	His	Pro	Ala	Gln	Tyr	Tyr	Pro	Ser	Pro
		35					40					45			
Val	Pro	Gln	Tyr	Ala	Pro	Arg	Val	Leu	Thr	Gln	Ala	Ser	Asn	Pro	Val
	50					55					60				
Val	Cys	Thr	Gln	Pro	Lys	Ser	Pro	Ser	Gly	Thr	Val	Cys	Thr	Ser	Lys
65					70					75					80
Thr	Lys	Lys	Ala	Leu	Cys	Ile	Thr	Leu	Thr	Leu	Gly	Thr	Phe	Leu	Val
				85					90					95	
Gly	Ala	Ala	Leu	Ala	Ala	Gly	Leu	Leu	Trp	Lys	Phe	Met	Gly	Ser	Lys
			100					105					110		
Cys	Ser	Asn	Ser	Gly	Ile	Glu	Cys	Asp	Ser	Ser	Gly	Thr	Cys	Ile	Asn
		115					120					125			
Pro	Ser	Asn	Trp	Cys	Asp	Gly	Val	Ser	His	Cys	Pro	Gly	Gly	Glu	Asp
		130				135					140				
Glu	Asn	Arg	Cys	Val	Arg	Leu	Tyr	Gly	Ser	Asn	Phe	Ile	Leu	Gln	Val
145					150					155					160
Tyr	Ser	Ser	Gln	Arg	Lys	Ser	Trp	His	Pro	Val	Cys	Gln	Asp	Asp	Trp
				165					170					175	
Asn	Glu	Asn	Tyr	Gly	Arg	Ala	Ala	Cys	Arg	Asp	Met	Gly	Tyr	Lys	Asn
			180					185					190		
Asn	Phe	Tyr	Ser	Ser	Gln	Gly	Ile	Val	Asp	Asp	Ser	Gly	Ser	Thr	Ser
		195				200					205				
Phe	Met	Lys	Leu	Asn	Thr	Ser	Ala	Gly	Asn	Val	Asp	Ile	Tyr	Lys	Lys
		210				215					220				
Leu	Tyr	His	Ser	Asp	Ala	Cys	Ser	Ser	Lys	Ala	Val	Val	Ser	Leu	Arg
225					230					235					240
Cys	Ile	Ala	Cys	Gly	Val	Asn	Leu	Asn	Ser	Ser	Arg	Gln	Ser	Arg	Ile
				245					250					255	
Val	Gly	Gly	Glu	Ser	Ala	Leu	Pro	Gly	Ala	Trp	Pro	Trp	Gln	Val	Ser
			260					265					270		
Leu	His	Val	Gln	Asn	Val	His	Val	Cys	Gly	Gly	Ser	Ile	Ile	Thr	Pro
		275					280					285			
Glu	Trp	Ile	Val	Thr	Ala	Ala	His	Cys	Val	Glu	Lys	Pro	Leu	Asn	Asn
					295						300				
Pro	Trp	His	Trp	Thr	Ala	Phe	Ala	Gly	Ile	Leu	Arg	Gln	Ser	Phe	Met
305					310					315					320
Phe	Tyr	Gly	Ala	Gly	Tyr	Gln	Val	Glu	Lys	Val	Ile	Ser	His	Pro	Asn
				325					330					335	
Tyr	Asp	Ser	Lys	Thr	Lys	Asn	Asn	Asp	Ile	Ala	Leu	Met	Lys	Leu	Gln
			340					345					350		
Lys	Pro	Leu	Thr	Phe	Asn	Asp	Leu</								

347

Cys Ala Lys Ala Tyr Arg Pro Gly Val Tyr Gly Asn Val Met Val Phe  
 465 470 475 480  
 Thr Asp Trp Ile Tyr Arg Gln Met Arg Ala Asp Gly  
 485 490

<210> 933  
 <211> 100  
 <212> PRT  
 <213> Homo sapiens

<400> 933  
 Met Ala Leu Asn Ser Gly Ser Pro Pro Ala Ile Gly Pro Tyr Tyr Glu  
 5 10 15  
 Asn His Gly Tyr Gln Pro Glu Asn Pro Tyr Pro Ala Gln Pro Thr Val  
 20 25 30  
 Val Pro Thr Val Tyr Glu Val His Pro Ala Gln Tyr Tyr Pro Ser Pro  
 35 40 45  
 Val Pro Gln Tyr Ala Pro Arg Val Leu Thr Gln Ala Ser Asn Pro Val  
 50 55 60  
 Val Cys Thr Gln Pro Lys Ser Pro Ser Gly Thr Val Cys Thr Ser Lys  
 65 70 75 80  
 Thr Lys Lys Ala Leu Cys Ile Thr Leu Thr Leu Gly Thr Phe Leu Val  
 85 90 95  
 Gly Ala Ala Leu  
 100

<210> 934  
 <211> 393  
 <212> PRT  
 <213> Homo sapiens

<400> 934  
 Leu Ala Ala Gly Leu Leu Trp Lys Phe Met Gly Ser Lys Cys Ser Asn  
 5 10 15  
 Ser Gly Ile Glu Cys Asp Ser Ser Gly Thr Cys Ile Asn Pro Ser Asn  
 20 25 30  
 Trp Cys Asp Gly Val Ser His Cys Pro Gly Gly Glu Asp Glu Asn Arg  
 35 40 45  
 Cys Val Arg Leu Tyr Gly Ser Asn Phe Ile Leu Gln Val Tyr Ser Ser  
 50 55 60  
 Gln Arg Lys Ser Trp His Pro Val Cys Gln Asp Asp Trp Asn Glu Asn  
 65 70 75 80  
 Tyr Gly Arg Ala Ala Cys Arg Asp Met Gly Tyr Lys Asn Asn Phe Tyr  
 85 90 95  
 Ser Ser Gln Gly Ile Val Asp Asp Ser Gly Ser Thr Ser Phe Met Lys  
 100 105 110  
 Leu Asn Thr Ser Ala Gly Asn Val Asp Ile Tyr Lys Lys Leu Tyr His  
 115 120 125  
 Ser Asp Ala Cys Ser Ser Lys Ala Val Val Ser Leu Arg Cys Ile Ala  
 130 135 140  
 Cys Gly Val Asn Leu Asn Ser Ser Arg Gln Ser Arg Ile Val Gly Gly  
 145 150 155 160  
 Glu Ser Ala Leu Pro Gly Ala Trp Pro Trp Gln Val Ser Leu His Val  
 165 170 175  
 Gln Asn Val His Val Cys Gly Gly Ser Ile Ile Thr Pro Glu Trp Ile  
 180 185 190

348

Val Thr Ala Ala His Cys Val Glu Lys, Pro Leu Asn Asn Pro Trp His  
 195 200 205  
 Trp Thr Ala Phe Ala Gly Ile Leu Arg Gln Ser Phe Met Phe Tyr Gly  
 210 215 220  
 Ala Gly Tyr Gln Val Glu Lys Val Ile Ser His Pro Asn Tyr Asp Ser  
 225 230 235 240  
 Lys Thr Lys Asn Asn Asp Ile Ala Leu Met Lys Leu Gln Lys Pro Leu  
 245 250 255  
 Thr Phe Asn Asp Leu Val Lys Pro Val Cys Leu Pro Asn Pro Gly Met  
 260 265 270  
 Met Leu Gln Pro Glu Gln Leu Cys Trp Ile Ser Gly Trp Gly Ala Thr  
 275 280 285  
 Glu Glu Lys Gly Lys Thr Ser Glu Val Leu Asn Ala Ala Lys Val Leu  
 290 295 300  
 Leu Ile Glu Thr Gln Arg Cys Asn Ser Arg Tyr Val Tyr Asp Asn Leu  
 305 310 315 320  
 Ile Thr Pro Ala Met Ile Cys Ala Gly Phe Leu Gln Gly Asn Val Asp  
 325 330 335  
 Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Thr Ser Lys Asn Asn  
 340 345 350  
 Ile Trp Trp Leu Ile Gly Asp Thr Ser Trp Gly Ser Gly Cys Ala Lys  
 355 360 365  
 Ala Tyr Arg Pro Gly Val Tyr Gly Asn Val Met Val Phe Thr Asp Trp  
 370 375 380  
 Ile Tyr Arg Gln Met Arg Ala Asp Gly  
 385 390

<210> 935  
 <211> 22  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> PCR Primer

<400> 935  
 gtgctgtggg agtccccgcg gc 22

<210> 936  
 <211> 36  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> PCR Primer

<400> 936  
 cgtgaactcg agtcattaga ttaacctcgt ggacgc 36

<210> 937  
 <211> 22  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> PCR Primer

349

<400> 937  
gtgctgtggg agtccccgcg gc

22

<210> 938  
<211> 1158  
<212> DNA  
<213> Homo sapiens

<400> 938  
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tggacacttt gcgagggtt ttgctggctg ctgctgctgc ccgtcatgct actcatcgta 120  
gcccccccg tgaagctcgc tgctttccct acctccttaa gtgactgcc aacgcccacc 180  
ggctggaatt gctctgggta tgatgacaga gaaaatgatc tcttcctctg tgacaccaac 240  
acctgtaaat ttgatgggga atgtttaaga attggagaca ctgtgacttg cgtctgtcag 300  
ttcaagtgca acaatgacta tgtgcctgtg tgtgggtcca atggggagag ctaccagaat 360  
gagtgttacc tgcgacaggc tgcattgcaa cagcagagtg agatacttgt ggtgtcagaa 420  
ggatcatgtg ccacagatgc aggatcagga tctggagatg gattccatga aggtctctga 480  
gaaactagtc aaaaggagac atccaactgt gatatttgcc agtttggtgc agaattgtac 540  
gaagatgccg aggatgtctg gtgtgtgtgt aatattgact gttctcaaac caacttcaat 600  
ccccctctgc cttctgatgg gaaatcttat gataatgcat gccaaatcaa agaagcatcg 660  
tgtcagaaac aggagaaaat tgaagtcatt tctttgggtc gatgtcaaga taacacaact 720  
acaactacta agtctgaaga tgggcattat gcaagaacag attatgcaga gaatgctaac 780  
aaattagaag aaagtgccag agaaccaccac ataccttgtc cggaacatta caatggcttc 840  
tgcattgcag ggaagtgtga gcattctatc aatatgcagg agccatcttg cagggtgtgat 900  
gctgggtata ctggacaaca ctgtgaaaaa aaggactaca gtgttctata cgttggtccc 960  
ggctctgtac gatattcagta tgtcttaatc gcagctgtga ttggaacaat tcagattgct 1020  
gtcatctgtg ttggtggctc ctgcatcaca aggaaatgcc ccagaagcaa cagaattcac 1080  
agacagaagc aaaatacagg gcactacagt tcagacaata caacaagagc gtccacgagg 1140  
ttaatctaata gactcgag 1158

<210> 939  
<211> 1020  
<212> DNA  
<213> Homo sapiens

<400> 939  
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tatgatgaca gagaaaatga tctcttcttc tgtgacacca acacctgtaa atttgatggg 120  
gaatgtttta gaattggaga cactgtgact tgcgtctgtc agttcaagt caacaatgac 180  
tatgtgcctg tgtgtggctc caatggggag agctaccaga atgagtgtta cctgcgacag 240  
gctgcatgca aacagcagag tgagatactt gtggtgtcag aaggatcatg tgccacagat 300  
gcaggatcag gatctggaga tggagtccat gaaggctctg gagaaactag tcaaaaggag 360  
acatccacct gtgatatttg ccagtttggt gcagaatgtg acgaagatgc cgaggatgtc 420  
tgggtgtgtg gtaatatatt ctgttctcaa accaacttca atccccctct cgcttctgat 480  
gggaaatctt atgataatgc atgcccattc aaagaagcat cgtgtcagaa acaggagaaa 540  
attgaagtca tgtctttggg tcgatgtcaa gataacacaa ctacaactac taagtctgaa 600  
gatgggcatt atgcaagaac agattatgca agaatgtcta acaaataga agaaagtgcc 660  
agagaacacc acataccttg tccggaacat tacaatggct tctgcatgca tgggaagtgt 720  
gagcattcta tcaatatgca ggagccatct tgcaggtgtg atgctgggta tactggacaa 780  
cactgtgaaa aaaaggacta cagtgttcta tacgttgttc ccggtcctgt acgatttcag 840  
tatgtcttaa tcgcagctgt gattggaaca attcagattg ctgtcatctg tgtgggtggc 900  
ctctgcatca caaggaaatg cccagaaagc aacagaattc acagacagaa gcaaaatata 960  
gggcactaca gttcagacaa tacaacaaga gcgtccacga ggtaaatcta atgactcgag 1020

<210> 940  
<211> 336

350

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 940

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Met Gln His His His His His His Asp Cys Gln Thr Pro Thr Gly Trp
                    5              10              15
Asn Cys Ser Gly Tyr Asp Asp Arg Glu Asn Asp Leu Phe Leu Cys Asp
          20              25              30
Thr Asn Thr Cys Lys Phe Asp Gly Glu Cys Leu Arg Ile Gly Asp Thr
          35              40              45
Val Thr Cys Val Cys Gln Phe Lys Cys Asn Asn Asp Tyr Val Pro Val
          50              55              60
Cys Gly Ser Asn Gly Glu Ser Tyr Gln Asn Glu Cys Tyr Leu Arg Gln
          65              70              75              80
Ala Ala Cys Lys Gln Gln Ser Glu Ile Leu Val Val Ser Glu Gly Ser
          85              90              95
Cys Ala Thr Asp Ala Gly Ser Gly Ser Gly Asp Gly Val His Glu Gly
          100             105             110
Ser Gly Glu Thr Ser Gln Lys Glu Thr Ser Thr Cys Asp Ile Cys Gln
          115             120             125
Phe Gly Ala Glu Cys Asp Glu Asp Ala Glu Asp Val Trp Cys Val Cys
          130             135             140
Asn Ile Asp Cys Ser Gln Thr Asn Phe Asn Pro Leu Cys Ala Ser Asp
          145             150             155             160
Gly Lys Ser Tyr Asp Asn Ala Cys Gln Ile Lys Glu Ala Ser Cys Gln
          165             170             175
Lys Gln Glu Lys Ile Glu Val Met Ser Leu Gly Arg Cys Gln Asp Asn
          180             185             190
Thr Thr Thr Thr Thr Lys Ser Glu Asp Gly His Tyr Ala Arg Thr Asp
          195             200             205
Tyr Ala Glu Asn Ala Asn Lys Leu Glu Glu Ser Ala Arg Glu His His
          210             215             220
Ile Pro Cys Pro Glu His Tyr Asn Gly Phe Cys Met His Gly Lys Cys
          225             230             235             240
Glu His Ser Ile Asn Met Gln Glu Pro Ser Cys Arg Cys Asp Ala Gly
          245             250             255
Tyr Thr Gly Gln His Cys Glu Lys Lys Asp Tyr Ser Val Leu Tyr Val
          260             265             270
Val Pro Gly Pro Val Arg Phe Gln Tyr Val Leu Ile Ala Ala Val Ile
          275             280             285
Gly Thr Ile Gln Ile Ala Val Ile Cys Val Val Val Leu Cys Ile Thr
          290             295             300
Arg Lys Cys Pro Arg Ser Asn Arg Ile His Arg Gln Lys Gln Asn Thr
          305             310             315             320
Gly His Tyr Ser Ser Asp Asn Thr Thr Arg Ala Ser Thr Arg Leu Ile
          325             330             335

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&lt;210&gt; 941

&lt;211&gt; 381

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 941

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Met Gln His His His His His His Val Leu Trp Glu Ser Pro Arg Gln
                    5              10              15
Cys Ser Ser Trp Thr Leu Cys Glu Gly Phe Cys Trp Leu Leu Leu Leu
          20              25              30

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351

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Pro Val Met Leu Leu Ile Val Ala Arg Pro Val Lys Leu Ala Ala Phe
      35      40      45
Pro Thr Ser Leu Ser Asp Cys Gln Thr Pro Thr Gly Trp Asn Cys Ser
      50      55      60
Gly Tyr Asp Asp Arg Glu Asn Asp Leu Phe Leu Cys Asp Thr Asn Thr
      65      70      75      80
Cys Lys Phe Asp Gly Glu Cys Leu Arg Ile Gly Asp Thr Val Thr Cys
      85      90      95
Val Cys Gln Phe Lys Cys Asn Asn Asp Tyr Val Pro Val Cys Gly Ser
      100      105      110
Asn Gly Glu Ser Tyr Gln Asn Glu Cys Tyr Leu Arg Gln Ala Ala Cys
      115      120      125
Lys Gln Gln Ser Glu Ile Leu Val Val Ser Glu Gly Ser Cys Ala Thr
      130      135      140
Asp Ala Gly Ser Gly Ser Gly Asp Gly Val His Glu Gly Ser Gly Glu
      145      150      155      160
Thr Ser Gln Lys Glu Thr Ser Thr Cys Asp Ile Cys Gln Phe Gly Ala
      165      170      175
Glu Cys Asp Glu Asp Ala Glu Asp Val Trp Cys Val Cys Asn Ile Asp
      180      185      190
Cys Ser Gln Thr Asn Phe Asn Pro Leu Cys Ala Ser Asp Gly Lys Ser
      195      200      205
Tyr Asp Asn Ala Cys Gln Ile Lys Glu Ala Ser Cys Gln Lys Gln Glu
      210      215      220
Lys Ile Glu Val Met Ser Leu Gly Arg Cys Gln Asp Asn Thr Thr Thr
      225      230      235      240
Thr Thr Lys Ser Glu Asp Gly His Tyr Ala Arg Thr Asp Tyr Ala Glu
      245      250      255
Asn Ala Asn Lys Leu Glu Glu Ser Ala Arg Glu His His Ile Pro Cys
      260      265      270
Pro Glu His Tyr Asn Gly Phe Cys Met His Gly Lys Cys Glu His Ser
      275      280      285
Ile Asn Met Gln Glu Pro Ser Cys Arg Cys Asp Ala Gly Tyr Thr Gly
      290      295      300
Gln His Cys Glu Lys Lys Asp Tyr Ser Val Leu Tyr Val Val Pro Gly
      305      310      315      320
Pro Val Arg Phe Gln Tyr Val Leu Ile Ala Ala Val Ile Gly Thr Ile
      325      330      335
Gln Ile Ala Val Ile Cys Val Val Val Leu Cys Ile Thr Arg Lys Cys
      340      345      350
Pro Arg Ser Asn Arg Ile His Arg Gln Lys Gln Asn Thr Gly His Tyr
      355      360      365
Ser Ser Asp Asn Thr Thr Arg Ala Ser Thr Arg Leu Ile
      370      375      380

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&lt;210&gt; 942

&lt;211&gt; 45

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 942

ctgctggcga acggcagaat gcctaccgtg ctgcagtgcg tgaac

45

&lt;210&gt; 943

&lt;211&gt; 15

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens



&lt;400&gt; 943

Leu Leu Ala Asn Gly Arg Met Pro Thr Val Leu Gln Cys Val Asn  
5 10 15

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